





# **STIC Search Report**

## **Biotech-Chem Library**

**STIC Database Tracking Number: 97818**

**TO: Leigh Maier**  
**Location: 7a03 / 8b19**  
**Sunday, July 06, 2003**  
**Art Unit: 1623**  
**Phone: 308-4525**  
**Serial Number: 10 / 069280**

**From: Jan Delaval**  
**Location: Biotech-Chem Library**  
**CM1-1E07**  
**Phone: 308-4498**

**jan.delaval@uspto.gov**

### **Search Notes**

Jan Delaval  
Reference Librarian  
Biotechnology & Chemical Library  
CM1 1E07 - 703-308-4498  
jan.delaval@uspto.gov

=> fil reg

FILE 'REGISTRY' ENTERED AT 16:47:23 ON 06 JUL 2003

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 4 JUL 2003 HIGHEST RN 542812-68-0

DICTIONARY FILE UPDATES: 4 JUL 2003 HIGHEST RN 542812-68-0

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

Please note that search-term pricing does apply when conducting SmartSELECT searches.

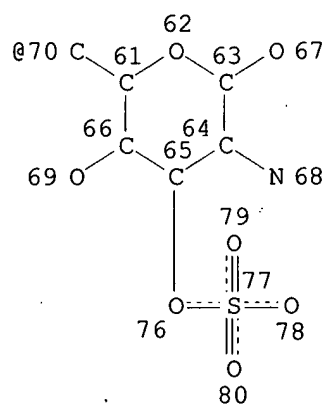
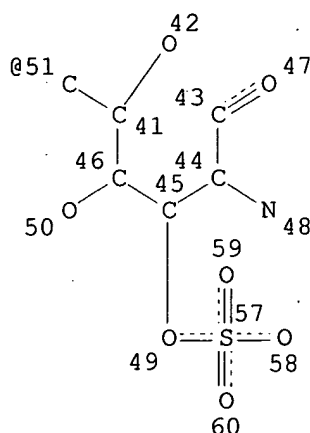
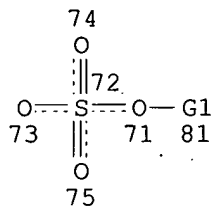
Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:

<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=> d sta que 171

L66 STR



VAR G1=51/70

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

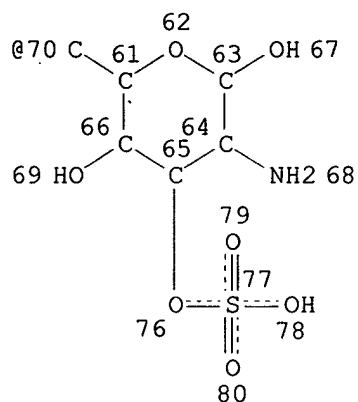
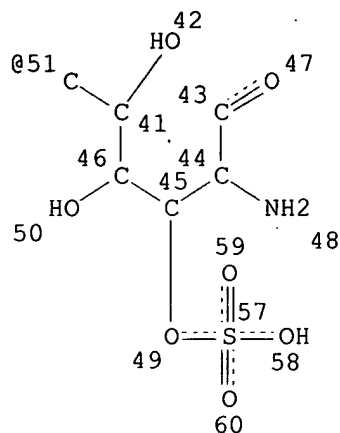
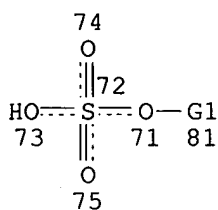
NUMBER OF NODES IS 36

STEREO ATTRIBUTES: NONE

L68 224 SEA FILE=REGISTRY SSS FUL L66

L69 STR

Jan Delaval  
Reference Librarian  
Biotechnology & Chemical Library  
CM1 1E07 - 703-308-4498  
[jan.delaval@uspto.gov](mailto:jan.delaval@uspto.gov)



VAR G1=51/70  
 NODE ATTRIBUTES:  
 DEFAULT MLEVEL IS ATOM  
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
 RING(S) ARE ISOLATED OR EMBEDDED  
 NUMBER OF NODES IS 36

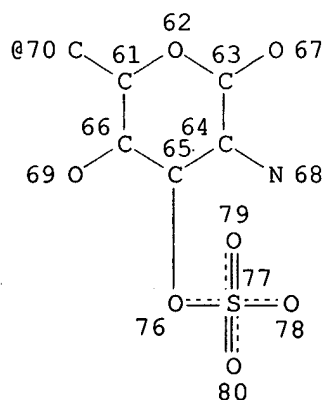
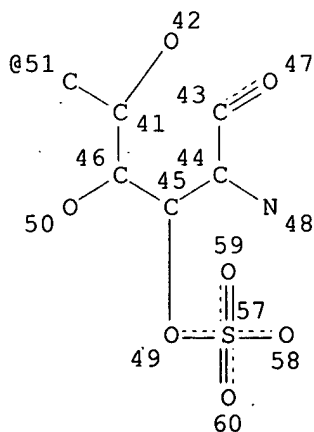
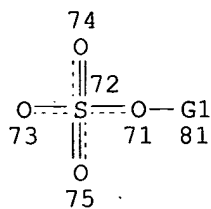
STEREO ATTRIBUTES: NONE  
 L71 4 SEA FILE=REGISTRY SUB=L68 SSS FUL L69

100.0% PROCESSED 224 ITERATIONS  
 SEARCH TIME: 00.00.01

4 ANSWERS

=> d sta que 175

L62 9 SEA FILE=REGISTRY ABB=ON PLU=ON C6H13NO11S2/MF  
 L63 3 SEA FILE=REGISTRY ABB=ON PLU=ON L62 NOT SULFOAMINO  
 L64 2 SEA FILE=REGISTRY ABB=ON PLU=ON L63 NOT IDS/CI  
 L65 1 SEA FILE=REGISTRY ABB=ON PLU=ON L64 AND 3  
 L66 STR



VAR G1=51/70  
 NODE ATTRIBUTES:  
 DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

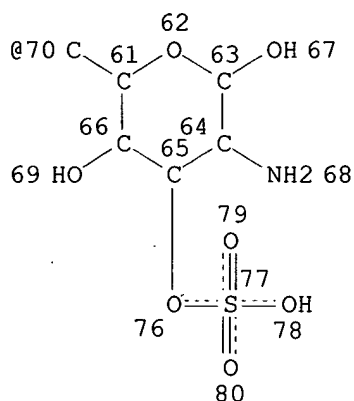
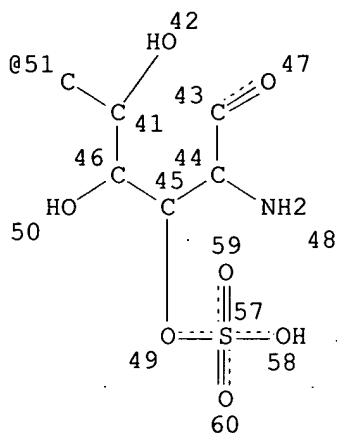
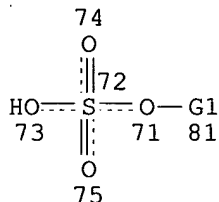
RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 36

STEREO ATTRIBUTES: NONE

L68 224 SEA FILE=REGISTRY SSS FUL L66

L69 STR



VAR G1=51/70

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

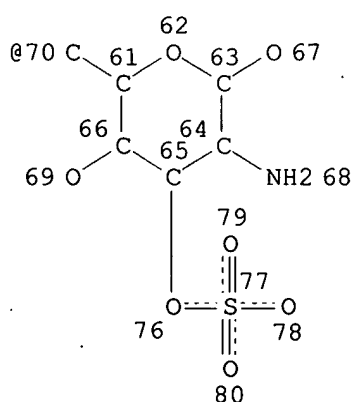
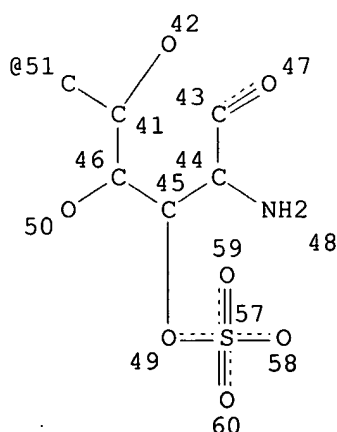
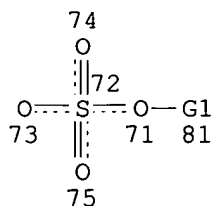
RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 36

STEREO ATTRIBUTES: NONE

L71 4 SEA FILE=REGISTRY SUB=L68 SSS FUL L69

L72 STR



VAR G1=51/70

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

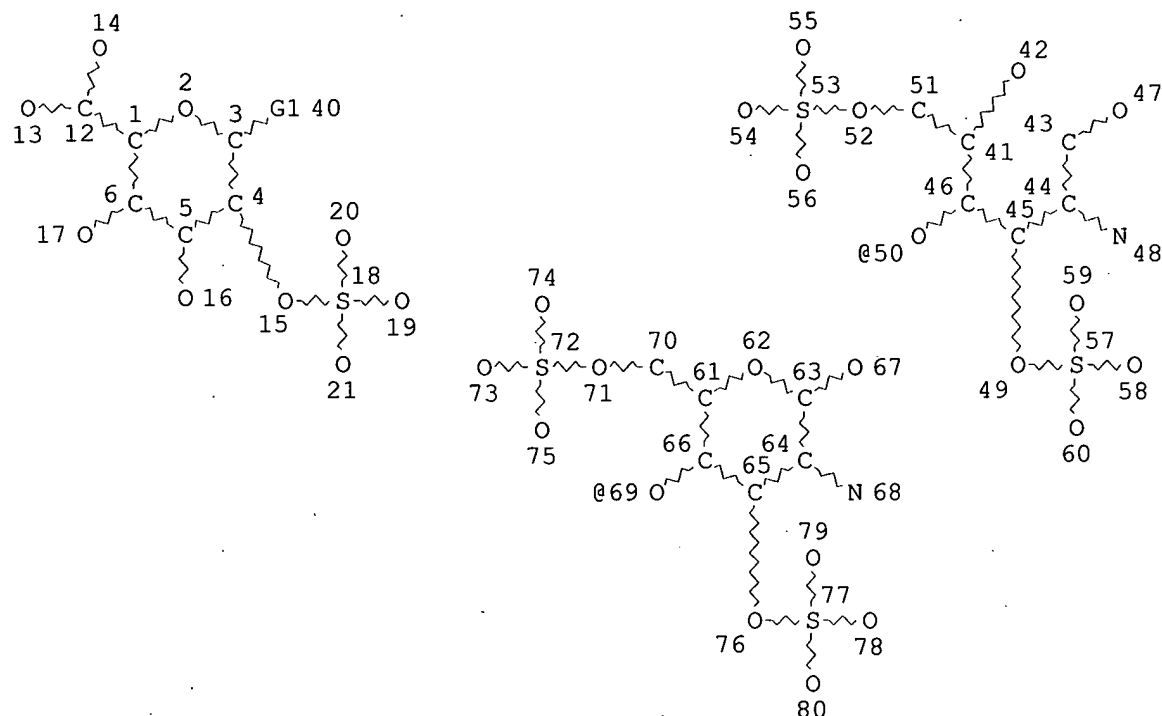
GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 36

STEREO ATTRIBUTES: NONE

L73 30 SEA FILE=REGISTRY SUB=L68 SSS FUL L72  
L74 26 SEA FILE=REGISTRY ABB=ON PLU=ON L73 NOT (L71 OR L65)  
L75 1 SEA FILE=REGISTRY ABB=ON PLU=ON L74 AND C12H21NO2OS3

=> d sta que 161  
L58 STR



VAR G1=50/69  
NODE ATTRIBUTES:  
DEFAULT MLEVEL IS ATOM  
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 57

STEREO ATTRIBUTES: NONE

L60 16 SEA FILE=REGISTRY SSS FUL L58  
L61 1 SEA FILE=REGISTRY ABB=ON PLU=ON L60 AND C12H21NO2OS3

=> d his

(FILE 'HOME' ENTERED AT 14:58:12 ON 06 JUL 2003)  
SET COST OFF

FILE 'HCAPLUS' ENTERED AT 14:58:22 ON 06 JUL 2003  
E WO2000-US23288/AP, PRN

L1 1 S E3  
E US99-150743/AP, PRN  
L2 1 S E5

E US2000-175347/AP, PRN  
L3 1 S E5  
L4 1 S L1-L3  
E SHUKLA D/AU  
L5 168 S E3-E12, E15, E16  
E ROSENBERG R/AU  
L6 2 S E3, E4  
E ROSENBERG R/AU  
L7 402 S E3, E8, E34, E40  
E SPEAR P/AU  
L8 142 S E3, E6, E9, E10  
L9 1 S L4 AND L5-L8  
SEL RN

FILE 'REGISTRY' ENTERED AT 15:02:48 ON 06 JUL 2003

L10 14 S E1-E14  
L11 6 S 67-68-5 OR 57-55-6 OR 67-63-0 OR 64-17-5 OR 112-80-1 OR 872-5  
L12 1 S 9050-30-0  
L13 14 S (70226-44-7 AND 7664-93-9)/CRN  
L14 3 S L13 AND (CA OR NA OR K)/ELS AND 3/NC  
L15 4 S L12, L14  
L16 7 S L10 NOT L11-L15  
L17 3 S L16 AND SQL/FA  
L18 4 S L16 NOT L17  
L19 1 S L18 AND UNSPECIFIED  
L20 3 S L18 NOT L19

FILE 'HCAPLUS' ENTERED AT 15:11:23 ON 06 JUL 2003

L21 703 S L5-L8 NOT L9

FILE 'HCAPLUS' ENTERED AT 15:11:31 ON 06 JUL 2003

SET SMARTSELECT ON  
L22 SEL L21 1- RN : 1245 TERMS  
SET SMARTSELECT OFF

FILE 'HCAPLUS' ENTERED AT 15:12:08 ON 06 JUL 2003

L24 703 S L21 OR L21  
SEL AN L24 1-200  
L25 200 S E15-E406  
SEL AN L24 201-400  
L26 200 S E407-E803  
DEL SEL  
SEL AN L24 401-600  
L27 200 S E1-E400  
SEL AN L24 601-703  
L28 103 S E401-E606

FILE 'REGISTRY' ENTERED AT 15:15:14 ON 06 JUL 2003

FILE 'HCAPLUS' ENTERED AT 15:15:14 ON 06 JUL 2003

SET SMARTSELECT ON  
L29 SEL L25 1- RN : 751 TERMS  
SET SMARTSELECT OFF

FILE 'REGISTRY' ENTERED AT 15:15:16 ON 06 JUL 2003

L30 751 S L29

FILE 'HCAPLUS' ENTERED AT 15:15:29 ON 06 JUL 2003

SET SMARTSELECT ON  
L31 SEL L26 1- RN : 321 TERMS  
SET SMARTSELECT OFF

FILE 'REGISTRY' ENTERED AT 15:15:31 ON 06 JUL 2003

L32 322 S L31

FILE 'HCAPLUS' ENTERED AT 15:15:40 ON 06 JUL 2003  
SET SMARTSELECT ON

L33 SEL L27 1- RN : 246 TERMS  
SET SMARTSELECT OFF

FILE 'REGISTRY' ENTERED AT 15:15:41 ON 06 JUL 2003

L34 246 S L33

FILE 'HCAPLUS' ENTERED AT 15:15:49 ON 06 JUL 2003  
SET SMARTSELECT ON

L35 SEL L28 1- RN : 108 TERMS  
SET SMARTSELECT OFF

FILE 'REGISTRY' ENTERED AT 15:15:50 ON 06 JUL 2003

L36 108 S L35  
L37 1245 S L30, L32, L34, L36  
L38 1241 S L37 NOT L10  
L39 58 S L38 AND OC5/ES  
L40 188 S L38 AND S/ELS  
L41 333 S L38 AND UNSPECIFIED  
L42 144 S L41 NOT SQL/FA  
L43 8 S L42 AND SULFOTRANSFERASE  
L44 1 S L43 AND 3  
L45 184 S L40 NOT L41  
L46 54 S L45 AND L39  
L47 14 S L46 NOT SULFOAMINO  
L48 1 S L47 AND C12H21NO14S  
L49 130 S L45 NOT L46  
L50 96 S L49 NOT SQL/FA  
L51 4 S L39 NOT L46-L50  
L52 5 S L38 AND ?GLUC?/CNS NOT L39-L51  
L53 1 S L20 AND OC5/ES  
L54 STR  
L55 0 S L54  
L56 STR L54  
L57 0 S L56  
L58 STR L56  
L59 0 S L58  
L60 16 S L58 FUL  
SAV L60 MAIER069/A  
L61 1 S L60 AND C12H21NO20S3  
SAV L61 MAIER069A/A  
E C6H13NO11S2/MF  
L62 9 S E3  
L63 3 S L62 NOT SULFOAMINO  
L64 2 S L63 NOT IDS/CI  
L65 1 S L64 AND 3  
L66 STR L58  
L67 9 S L66  
L68 224 S L66 FUL  
SAV L68 MAIER069B/A  
L69 STR L66  
L70 0 S L69 SAM SUB=L68  
L71 4 S L69 FUL SUB=L68  
SAV L71 MAIER069C/A  
L72 STR L69  
L73 30 S L72 FUL SUB=L68  
SAV L73 MAIER069D/A  
L74 26 S L73 NOT L71, L65  
L75 1 S L74 AND C12H21NO20S3



FILE 'HCAPLUS' ENTERED AT 16:04:08 ON 06 JUL 2003

L76 5 S L61,L65,L75  
L77 2 S L76 AND (PY<=1999 OR PRY<=1999 OR AY<=1999)  
L78 19 S 3 OST  
L79 67 S 3 O ( ) (SULFOTRANSFERASE OR SULPHOTRANSFERASE OR (SULFO OR SUL  
L80 70 S L78,L79  
L81 5 S L80 (L) 3A  
L82 4 S L80 (L) 3B  
L83 7 S L81,L82  
L84 21 S L80 AND L12  
L85 40 S L80 AND HEPARAN ( ) (SULFATE OR SULPHATE)  
L86 40 S L84,L85  
L87 4 S 3OST#  
L88 42 S L83,L86,L87  
L89 42 S L80 AND L88  
L90 28 S L80 NOT L89  
L91 1 S L90 AND HERPES SIMPLEX  
SEL RN L89  
DEL SEL

FILE 'REGISTRY' ENTERED AT 16:12:03 ON 06 JUL 2003

FILE 'HCAPLUS' ENTERED AT 16:12:03 ON 06 JUL 2003

SET SMARTSELECT ON  
L92 SEL L89.1- RN : 4962 TERMS  
SET SMARTSELECT OFF

FILE 'REGISTRY' ENTERED AT 16:12:06 ON 06 JUL 2003

L93 4962 S L92  
L94 63 S L93 AND (?SULFOTRANSFERASE? OR ?SULPHOTRANSFERASE?)/CNS  
L95 61 S L94 AND (SULFOTRANSFERASE OR SULPHOTRANSFERASE)/INS.HP  
L96 2 S L94 NOT L95  
L97 47 S L95 AND 3  
L98 13 S L95 AND (3A OR 3B)  
L99 47 S L97,L98  
L100 14 S L95 NOT L99  
L101 41 S L99 AND (3 OR 3A OR 3B)/INS.HP  
L102 6 S L99 NOT L101  
L103 2 S L102 NOT (SQL/FA OR STEROID)  
L104 38 S L101 AND HEPAR?  
L105 3 S L101 NOT L104  
L106 2 S L105 AND 3 O  
L107 19 S L104 AND 3 O  
L108 1 S L107 NOT (CLONE OR MUS OR MOUSE)  
L109 19 S L104 NOT L107  
L110 2 S L19,L103  
L111 909 S SULFOTRANSFERASE OR SULPHOTRANSFERASE  
L112 846 S L111 NOT L94  
L113 136 S L112 AND 3  
L114 13 S L112 AND 3 O  
L115 123 S L113 NOT L114  
L116 0 S L112 AND (3A OR 3B)

FILE 'HCAPLUS' ENTERED AT 16:22:51 ON 06 JUL 2003

L117 34 S L110  
L118 31 S L117 AND L78-L90  
L120 15 S HEPARAN ( ) (SULFATE OR SULPHATE) ( ) (3 OR 3 O) ( ) (SULFOTRANSFERASE  
L121 73 S L78-L90,L117-L120  
L122 6 S L121 AND ?HERPE?  
E HERPES/CT  
E E31+ALL  
L123 2969 S E2  
E E2+ALL

L124 4254 S E8  
L125 9 S E6  
E E6+ALL  
L126 7223 S E9,E12  
E E9+ALL  
L127 10903 S E7,E9-E26/BI  
L128 4250 S L12  
L129 7432 S HEPARAN() (SULFATE OR SULPHATE)  
L130 11444 S L123-L127  
L131 39 S L130 AND L128  
L132 82 S L130 AND L129  
L133 1 S L77 AND L121  
L134 1 S L77 AND L130  
L135 2 S L77,L133,L134  
E GLYCOPROTEIN/CT  
L136 691 S E186,E187  
L137 1024 S (GLYCOPROTEIN OR GP) (L)GD  
L138 3 S L136,L137 AND L121  
L139 672 S L136,L137 AND L130  
L140 926 S L136,L137 AND (?HERPE? OR HSV?)  
L141 708 S L139,L140 AND (PY<=1999 OR PRY<=1999 OR AY<=1999)  
L142 0 S L141 AND (OVERSULFAT? OR OVERSULPHAT?)  
E SULFATION/CT  
E E3+ALL  
L143 1 S L141 AND E3  
L144 28 S L141 AND ?SACCHARIDE?  
L145 130 S L5-L8 AND (?HERPE? OR HSV? OR L123-L127)  
L146 6 S L145 AND ?SACCHARID?  
L147 15 S L145 AND L128,L129  
L148 4 S L145 AND L121  
L149 19 S L146-L148  
L150 15 S L149 AND (PY<=1999 OR PRY<=1999 OR AY<=1999)  
L151 4 S L149 NOT L150  
L152 20 S L150,L151,L135  
L153 111 S L145 NOT L152  
L154 10 S L152 AND (D OR GD)  
L155 10 S L152 NOT L154  
L156 163 S L129,L128 AND E3+NT  
L157 2 S L156 AND L123-L127  
L158 2 S L156 AND (?HERPE? OR HSV?)  
L159 2 S L157,L158  
L160 11 S L159,L154

FILE 'REGISTRY' ENTERED AT 16:47:23 ON 06 JUL 2003

=> fil hcaplus

FILE 'HCAPLUS' ENTERED AT 16:48:24 ON 06 JUL 2003

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FILE COVERS 1907 - 6 Jul 2003 VOL 139 ISS 2

FILE LAST UPDATED: 4 Jul 2003 (20030704/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d 1160 all hitstr tot

L160 ANSWER 1 OF 11 HCAPLUS COPYRIGHT 2003 ACS  
AN 2002:743069 HCAPLUS  
DN 138:102854  
TI **Heparan Sulfate 3-O-Sulfotransferase** Isoform 5 Generates Both an Antithrombin-Binding Site and an Entry Receptor for **Herpes Simplex Virus, Type 1**  
AU Xia, Guoqing; Chen, Jinghua; Tiwari, Vaibhav; Ju, Wujian; Li, Jin-Ping; Malmstrom, Anders; **Shukla, Deepak**; Liu, Jian  
CS Cell and Molecular Biology, Biomedical Center C13, Lund University, Lund, S-22184, Swed.  
SO Journal of Biological Chemistry (2002), 277(40), 37912-37919  
CODEN: JBCHA3; ISSN: 0021-9258  
PB American Society for Biochemistry and Molecular Biology  
DT Journal  
LA English  
CC 7-5 (Enzymes)  
Section cross-reference(s): 6, 10  
AB **Heparan sulfate 3-O-sulfotransferase** transfers sulfate to the 3-OH position of a glucosamine residue of **heparan sulfate** (HS) to form 3-O-sulfated HS. The 3-O-sulfated glucosamine residue contributes to two important biol. functions of HS: binding to antithrombin and thereby carrying anticoagulant activity, and binding to **herpes simplex** viral envelope glycoprotein D to serve as an entry receptor for **herpes simplex virus 1**. A total of five HS 3-O-sulfotransferase isoforms were reported previously. Here we report the isolation and characterization of a novel HS 3-O-sulfotransferase isoform, designated as HS 3-O-sulfotransferase isoform 5 (3-OST-5). 3-OST-5 cDNA was isolated from a human placenta cDNA library and expressed in COS-7 cells. The **disaccharide** anal. of 3-OST-5-modified HS revealed that 3-OST-5 generated at least three 3-O-sulfated **disaccharides** as follows: IdoUA2S-AnMan3S, GlcUA-AnMan3S6S, and IdoUA2S-AnMan3S6S. Transfection of the plasmid expressing 3-OST-5 rendered wild type Chinese hamster ovary cells susceptible to the infection by **herpes simplex virus 1**, suggesting that 3-OST-5-modified HS serves as an entry receptor for **herpes simplex virus 1**. In addn., 3-OST-5-modified HS bound to **herpes simplex** viral envelope protein glycoprotein D. Furthermore, we found that 3-OST-5-modified HS also bound to antithrombin, suggesting that 3-OST-5 also produces anticoagulant HS. In summary, our results indicate that a new member of 3-OST family generates both anticoagulant HS and an entry receptor for **herpes simplex virus 1**. These results provide a new insight regarding the mechanism for the biosynthesis of biol. active HS.  
ST sulfotransferase 5 **heparan sulfate** protein sequence;  
**heparan sulfate** human **herpes simplex virus 1** receptor antithrombin  
IT Envelope proteins  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(D; **heparan sulfate** modification by

- heparan sulfate 3-O-sulfotransferase isoform 5 resulting in antithrombin and herpes simplex virus 1 binding)**
- IT Human  
Muscle  
Protein sequences  
Transcriptional regulation  
cDNA sequences  
(cloning sequencing and tissue expression of human **heparan sulfate 3-O-sulfotransferase isoform 5 cDNA)**
- IT Protein motifs  
(glycosylation site; cloning sequencing and tissue expression of human **heparan sulfate 3-O-sulfotransferase isoform 5 cDNA)**
- IT Anticoagulants  
**Human herpesvirus 1**  
Molecular association  
(**heparan sulfate** modification by **heparan sulfate 3-O-sulfotransferase isoform 5 resulting in antithrombin and herpes simplex virus 1 binding)**)
- IT Protein motifs  
(transmembrane domain; cloning sequencing and tissue expression of human **heparan sulfate 3-O-sulfotransferase isoform 5 cDNA)**
- IT 119692-05-6 130795-98-1 488704-69-4  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(HS fragment; **heparan sulfate** modification by **heparan sulfate 3-O-sulfotransferase isoform 5 resulting in antithrombin and herpes simplex virus 1 binding)**)
- IT 479474-87-8  
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
(amino acid sequence; cloning sequencing and tissue expression of human **heparan sulfate 3-O-sulfotransferase isoform 5 cDNA)**)
- IT 9000-94-6, Antithrombin  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(**heparan sulfate** modification by **heparan sulfate 3-O-sulfotransferase isoform 5 resulting in antithrombin and herpes simplex virus 1 binding)**)
- IT 9050-30-0, Heparan sulfate  
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
(**heparan sulfate** modification by **heparan sulfate 3-O-sulfotransferase isoform 5 resulting in antithrombin and herpes simplex virus 1 binding)**)
- IT 183257-54-7, Heparan sulfate 3-O-sulfotransferase  
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
(isoform 5; cloning sequencing and tissue expression of human **heparan sulfate 3-O-sulfotransferase isoform 5 cDNA)**)
- IT 459780-76-8  
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
(nucleotide sequence; cloning sequencing and tissue expression of human **heparan sulfate 3-O-**

**sulfotransferase isoform 5 cDNA)**

RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD  
RE

- (1) Aikawa, J; J Biol Chem 2001, V276, P5876 HCAPLUS
- (2) Akkaraju, G; J Gene Med 1999, V1, P280 MEDLINE
- (3) Alexander, C; Nat Genet 2000, V25, P329 HCAPLUS
- (4) Bernfield, M; Annu Rev Biochem 1999, V68, P729 HCAPLUS
- (5) Bjornsson, S; Anal Biochem 1993, V210, P282 MEDLINE
- (6) Carfi, A; Mol Cell 2001, V8, P169 HCAPLUS
- (7) Dennissen, M; J Biol Chem 2002, V277, P10982 HCAPLUS
- (8) Esko, J; J Clin Invest 2001, V108, P169 HCAPLUS
- (9) Grobe, K; J Biol Chem 2002, V277, P30699 HCAPLUS
- (10) Habuchi, H; J Biol Chem 2000, V275, P2859 HCAPLUS
- (11) Hernaiz, M; Biochem Biophys Res Commun 2000, V276, P292 HCAPLUS
- (12) Jenniskens, G; J Neurosci 2000, V20, P4099 HCAPLUS
- (13) Krummenacher, C; J Virol 1999, V73, P8127 HCAPLUS
- (14) Lindahl, U; J Biol Chem 1998, V273, P24979 HCAPLUS
- (15) Lindahl, U; Proc Natl Acad Sci 1980, V77, P6551 HCAPLUS
- (16) Liu, J; Handbook of Glycosyltransferases and Their Related Genes 2002, P475
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IT 9050-30-0, **Heparan sulfate**

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL  
(Biological study)

(**heparan sulfate** modification by **heparan  
sulfate 3-O-sulfotransferase**  
isoform 5 resulting in antithrombin and **herpes  
simplex virus 1** binding)

RN 9050-30-0 HCAPLUS

CN Heparan, sulfate (9CI) (CA INDEX NAME)

CM 1

CRN 70226-44-7

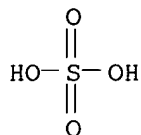
CMF Unspecified

CCI MAN

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

CM 2

CRN 7664-93-9  
CMF H2 O4 S



IT 183257-54-7, **Heparan sulfate 3-O-sulfotransferase**  
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
(isoform 5; cloning sequencing and tissue expression of human **heparan sulfate 3-O-sulfotransferase** isoform 5 cDNA)  
RN 183257-54-7 HCAPLUS  
CN Sulfotransferase, heparitin 3- (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

L160 ANSWER 2 OF 11 HCAPLUS COPYRIGHT 2003 ACS

AN 2001:775449 HCAPLUS

DN 136:33840

TI Portable sulphotransferase domain determines sequence specificity of **heparan sulphate 3-O-sulphotransferases**

AU Yabe, Tomio; Shukla, Deepak; Spear, Patricia G.;

Rosenberg, Robert D.; Seeberger, Peter H.; Shworak, Nicholas W.

CS Angiogenesis Research Center, Department of Medicine, Harvard Medical School, Beth Israel Deaconess Medical Center, Boston, MA, 02215, USA

SO Biochemical Journal (2001), 359(1), 235-241

CODEN: BIJOAK; ISSN: 0264-6021

PB Portland Press Ltd.

DT Journal

LA English

CC 7-5 (Enzymes)

AB 3-O-Sulfates are the rarest substituent of **heparan sulfate** and are therefore ideally suited to the selective regulation of biol. activities. Individual isoforms of **heparan sulfate D-glucosaminyl 3-O-sulfotransferase (3-OST)** exhibit sequence-specific action, which creates **heparan sulfate** structures with distinct biol. functions. For example, 3-OST-1 preferentially generates binding sites for anti-thrombin, whereas 3-OST-3 isoforms create binding sites for the gD envelope protein of **herpes simplex virus 1 (HSV-1)**, which enables viral entry. 3-OST enzymes comprise a presumptive sulfotransferase domain and a divergent N-terminal region. To localize determinants of sequence specificity, we conducted domain swaps between cDNA species. The N-terminal region of 3-OST-1 was fused with the sulfotransferase domain of 3-OST-3A to generate N1-ST3A. Similarly, the N-terminal region of 3-OST-3A was fused to the sulfotransferase domain of 3-OST-1 to generate N3A-ST1. Wild-type and chimeric enzymes were transiently expressed in COS-7 cells and exts. were analyzed for selective generation of binding sites for anti-thrombin. 3-OST-1 was 270-fold more efficient at forming anti-thrombin-binding sites than 3-OST-3A,

indicating its significantly greater selectivity for substrates that can be 3-O-sulfated to yield such sites. N3A-ST1 was as active as 3-OST-1, whereas the activity of N1-ST3A was as low as that of 3-OST-3A. Anal. of Chinese hamster ovary cell transfectants revealed that only 3-OST-3A and N1-ST3A generated gD-binding sites and conveyed susceptibility to infection by HSV-1. Thus sequence-specific properties of 3-OSTs are defined by a self-contained sulfotransferase domain and are not directly influenced by the divergent N-terminal region.

ST sulfotransferase domain **heparan sulfate**

IT Protein sequences

(alignment, sulfotransferases; chimeric enzyme studies of sequence specificity of **heparan sulfate 3-O-sulfotransferases**)

IT Enzyme functional sites

(chimeric enzyme studies of sequence specificity of **heparan sulfate 3-O-sulfotransferases**)

IT 9000-94-6, Antithrombin

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(chimeric enzyme studies of sequence specificity of **heparan sulfate 3-O-sulfotransferases**)

IT 183257-54-7, **Heparan sulfate D**

-glucosaminyl **3-O-sulfotransferase**

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(chimeric enzyme studies of sequence specificity of **heparan sulfate 3-O-sulfotransferases**)

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IT 183257-54-7, **Heparan sulfate D**

-glucosaminyl 3-O-sulfotransferase

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(chimeric enzyme studies of sequence specificity of **heparan sulfate 3-O-sulfotransferases**)

RN 183257-54-7 HCAPLUS

CN Sulfotransferase, heparitin 3- (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

L160 ANSWER 3 OF 11 HCAPLUS COPYRIGHT 2003 ACS

AN 2001:620938 HCAPLUS

DN 135:342175

TI **Herpesviruses and heparan sulfate: an**  
intimate relationship in aid of viral entry

AU **Shukla, Deepak; Spear, Patricia G.**

CS Department of Microbiology-Immunology, Northwestern University Medical  
School, Chicago, IL, 60611, USA

SO Journal of Clinical Investigation (2001), 108(4), 503-510

CODEN: JCINAO; ISSN: 0021-9738

PB American Society for Clinical Investigation

DT Journal; General Review

LA English

CC 14-0 (Mammalian Pathological Biochemistry)

Section cross-reference(s): 10

AB A review with 52 refs. Topics discussed include the family of  
**herpesviruses**; clin. manifestations of **herpesvirus**  
diseases in humans; pathways of **herpesvirus** entry into cells;  
**heparan sulfate** as the initial receptor for the binding  
of **herpesviruses** to cells; mol. interactions between  
**herpesvirus** glycoproteins and **heparan sulfate**;  
**heparan sulfate** as an entry receptor; and implications  
of **herpesvirus** binding to **heparan sulfate**  
for pathogenesis.

ST review **herpesvirus** infection **heparan sulfate**

IT Glycoproteins, specific or class

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
(gB; interaction between **heparan sulfate** and viral  
surface glycoproteins in **herpesvirus** infection)

IT Glycoproteins, specific or class

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
(gC; interaction between **heparan sulfate** and viral  
surface glycoproteins in **herpesvirus** infection)

IT Glycoproteins, specific or class

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
(gD; interaction between **heparan sulfate**  
and viral surface glycoproteins in **herpesvirus** infection)

IT Human **herpesvirus**

(interaction between **heparan sulfate** and viral  
surface glycoproteins in **herpesvirus** infection)



## IT Infection

(viral; interaction between **heparan sulfate** and  
viral surface glycoproteins in **herpesvirus** infection)

IT 9050-30-0, **Heparan sulfate**

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
(interaction between **heparan sulfate** and viral  
surface glycoproteins in **herpesvirus** infection)

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IT 9050-30-0, **Heparan sulfate**

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)

(interaction between **heparan sulfate** and viral  
surface glycoproteins in **herpesvirus** infection)

RN 9050-30-0 HCAPLUS  
CN Heparan, sulfate (9CI) (CA INDEX NAME)

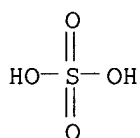
CM 1

CRN 70226-44-7  
CMF Unspecified  
CCI MAN

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

CM 2

CRN 7664-93-9  
CMF H2 O4 S



L160 ANSWER 4 OF 11 HCAPLUS COPYRIGHT 2003 ACS

AN 2001:152481 HCAPLUS

DN 134:212717

TI Pharmaceutical preparations for the inhibition of **herpes simplex virus 1** entry

IN Shukla, Deepak; Liu, Jian; Rosenberg, Robert D.;  
Spear, Patricia G.

PA Massachusetts Institute of Technology, USA; Northwestern University

SO PCT Int. Appl., 29 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K031-00

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001013910	A2	20010301	WO 2000-US23288	20000825 <--
	WO 2001013910	A3	20011101		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			

PRAI US 1999-150743P P 19990825 <--

US 2000-175347P P 20000110

AB Disclosed herein are **polysaccharide** preps. enriched in  
**3-OST-3** modified **heparan sulfate**.

Also disclosed are methods of treating **herpes simplex** viral  
type-1 infection using the pharmaceutical preps. of the invention.

ST **herpes HSV1** virustat **heparan sulfate**

- deriv
- IT Drug delivery systems  
(foams; **polysaccharide** preps. for the inhibition of  
**herpes simplex virus 1** entry)
- IT Glycoproteins, specific or class  
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)  
(gD; **polysaccharide** preps. for the inhibition of  
**herpes simplex virus 1** entry)
- IT Drug delivery systems  
(gels; **polysaccharide** preps. for the inhibition of  
**herpes simplex virus 1** entry)
- IT Drug delivery systems  
(liniments; **polysaccharide** preps. for the inhibition of  
**herpes simplex virus 1** entry)
- IT Drug delivery systems  
(lotions; **polysaccharide** preps. for the inhibition of  
**herpes simplex virus 1** entry)
- IT Drug delivery systems  
(ointments, creams; **polysaccharide** preps. for the inhibition  
of **herpes simplex virus 1**  
entry)
- IT Drug delivery systems  
(ointments; **polysaccharide** preps. for the inhibition of  
**herpes simplex virus 1** entry)
- IT Skin  
(permeation of; **polysaccharide** preps. for the inhibition of  
**herpes simplex virus 1** entry)
- IT Antiviral agents  
**Human herpesvirus 1**  
Molecular cloning  
Permeation enhancers  
Transformation, genetic  
(**polysaccharide** preps. for the inhibition of **herpes simplex virus 1** entry)
- IT **Polysaccharides**, biological studies  
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PROC (Process); USES (Uses)  
(**polysaccharide** preps. for the inhibition of **herpes simplex virus 1** entry)
- IT Drug delivery systems  
(slow-release, polymers; **polysaccharide** preps. for the  
inhibition of **herpes simplex virus 1** entry)
- IT Drug delivery systems  
(suppositories; **polysaccharide** preps. for the inhibition of  
**herpes simplex virus 1** entry)
- IT 183257-54-7, Heparan sulfate 3-sulfotransferase  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(isoform 3-OST-3; **polysaccharide** preps.  
for the inhibition of **herpes simplex virus 1** entry)
- IT 67-63-0, Isopropanol, biological studies 872-50-4, N-Methylpyrrolidone, biological studies  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(**polysaccharide** preps. for the inhibition of **herpes simplex virus 1** entry)

- IT 3416-24-8D, Glucosamine, sulfate derivs. 76330-21-7  
328085-46-7 328085-46-7D, glycoside derivs.  
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PROC (Process); USES (Uses)  
(polysaccharide preps. for the inhibition of herpes simplex virus 1 entry)
- IT 9050-30-0, Heparan sulfate  
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(polysaccharide preps. for the inhibition of herpes simplex virus 1 entry)
- IT 57-55-6, Propylene glycol, biological studies 64-17-5, Ethanol, biological studies 67-68-5, DmsO, biological studies 112-80-1, Oleic acid, biological studies  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(skin permeation enhancer; polysaccharide preps. for the inhibition of herpes simplex virus 1 entry)
- IT 328319-66-0 328319-67-1 328319-68-2  
RL: PRP (Properties)  
(unclaimed protein sequence; pharmaceutical preps. for the inhibition of herpes simplex virus 1 entry)

RE.CNT 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD  
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IT 183257-54-7, **Heparan sulfate 3-sulfotransferase**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study) (isoform 3-OST-3; **polysaccharide** preps. for the inhibition of **herpes simplex virus** 1 entry)

RN 183257-54-7 HCAPLUS

CN Sulfotransferase, heparitin 3- (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

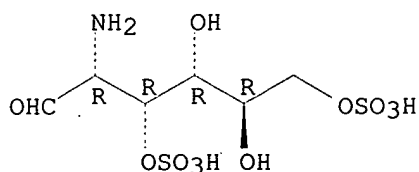
IT 76330-21-7 328085-46-7 328085-46-7D, glycoside derivs.

RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PROC (Process); USES (Uses) (**polysaccharide** preps. for the inhibition of **herpes simplex virus** 1 entry)

RN 76330-21-7 HCAPLUS

CN D-Glucose, 2-amino-2-deoxy-, 3,6-bis(hydrogen sulfate) (9CI) (CA INDEX NAME)

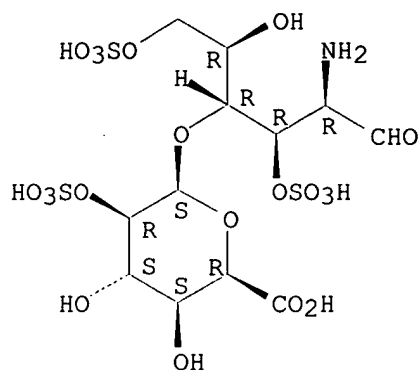
Absolute stereochemistry.



RN 328085-46-7 HCAPLUS

CN D-Glucose, 2-amino-2-deoxy-4-O-(2-O-sulfo-.beta.-L-idopyranuronosyl)-, 3,6-bis(hydrogen sulfate) (9CI) (CA INDEX NAME)

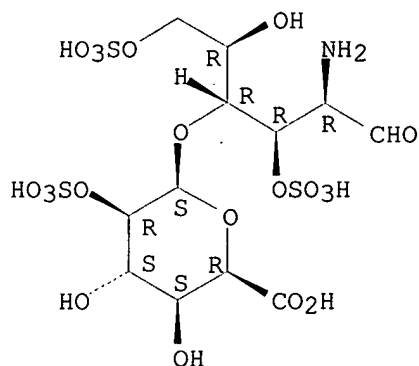
Absolute stereochemistry.



RN 328085-46-7 HCAPLUS

CN D-Glucose, 2-amino-2-deoxy-4-O-(2-O-sulfo-.beta.-L-idopyranuronosyl)-, 3,6-bis(hydrogen sulfate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 9050-30-0, Heparan sulfate

RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(polysaccharide preps. for the inhibition of herpes simplex virus 1 entry)

RN 9050-30-0 HCAPLUS

CN Heparan, sulfate (9CI) (CA INDEX NAME)

CM 1

CRN 70226-44-7

CMF Unspecified

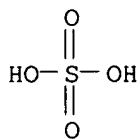
CCI MAN

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

CM 2

CRN 7664-93-9

CMF H2 O4 S



L160 ANSWER 5 OF 11 HCAPLUS COPYRIGHT 2003 ACS

AN 2001:16328 HCAPLUS

DN 134:219618

TI Cell fusion induced by **herpes** simplex virus glycoproteins gB, gD, and gH-gL requires a gD receptor but not necessarily **heparan sulfate**

AU Pertel, Peter E.; Fridberg, Alina; Parish, Mary L.; Spear, Patricia G.

CS Department of Medicine, Division of Infectious Diseases, Northwestern University Medical School, Chicago, IL, 60611, USA

SO Virology (2001), 279(1), 313-324

CODEN: VIRLAX; ISSN: 0042-6822

PB Academic Press

DT Journal

LA English

CC 10-6 (Microbial, Algal, and Fungal Biochemistry)

AB To characterize cellular factors required for **herpes**

**simplex virus type 1 (HSV-**

1)-induced cell fusion, we used an efficient and quant. assay relying on expression of **HSV-1** glycoproteins in transfected cells. We showed the following: (1) Cell fusion depended not only on expression of four viral glycoproteins (gB, gD, and gH-gL), as previously shown, but also on expression of cell surface entry receptors specific for gD. (2) Cell fusion required expression of all four glycoproteins in the same cell. (3) **Heparan sulfate** was not required for cell fusion. (4) Coexpression of receptor with the four glycoproteins in the same cell reduced fusion activity, indicating that interaction of gD and receptor can limit polykaryocyte formation. Overall, the viral and cellular determinants of **HSV-1**-induced cell fusion are similar to those for viral entry, except that **HSV-1** entry is significantly enhanced by binding of virus to cell surface **heparan sulfate**. (c) 2001 Academic Press.

ST **herpes** simplex virus glycoprotein cell fusion **heparan sulfate**

IT Cell fusion

**Human herpesvirus 1**

(cell fusion induced by **herpes** simplex virus glycoproteins gB, gD, and gH-gL requires gD receptor but not necessarily **heparan sulfate**)

IT Receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study) (cell fusion induced by **herpes** simplex virus glycoproteins gB, gD, and gH-gL requires gD receptor but not necessarily **heparan sulfate**)

IT Glycoproteins, specific or class

RL: BSU (Biological study, unclassified); BIOL (Biological study) (gB; cell fusion induced by **herpes** simplex virus glycoproteins gB, gD, and gH-gL requires gD receptor but not necessarily **heparan sulfate**)

IT Glycoproteins, specific or class

RL: BSU (Biological study, unclassified); BIOL (Biological study) (gD; cell fusion induced by **herpes** simplex virus glycoproteins gB, gD, and gH-gL requires gD

receptor but not necessarily **heparan sulfate**)  
IT Glycoproteins, specific or class  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(gH-gL; cell fusion induced by **herpes** simplex virus  
glycoproteins gB, gD, and gH-gL requires gD  
receptor but not necessarily **heparan sulfate**)  
IT 9050-30-0, **Heparan sulfate**  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(cell fusion induced by **herpes** simplex virus glycoproteins  
gB, gD, and gH-gL requires gD receptor but not  
necessarily **heparan sulfate**)

RE.CNT 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD  
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IT 9050-30-0, **Heparan sulfate**

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (cell fusion induced by **herpes** simplex virus glycoproteins  
 gB, gD, and gH-gL requires gD receptor but not  
 necessarily **heparan sulfate**)

RN 9050-30-0 HCAPLUS

CN Heparan, sulfate (9CI) (CA INDEX NAME)

CM 1

CRN 70226-44-7

CMF Unspecified

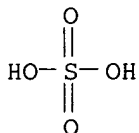
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\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

CM 2

CRN 7664-93-9

CMF H2 O4 S



L160 ANSWER 6 OF 11 HCAPLUS COPYRIGHT 2003 ACS

AN 1999:673913 HCAPLUS

DN 132:21694

TI A novel role for 3-O-sulfated **heparan sulfate** in  
**herpes simplex virus 1** entry

AU Shukla, Deepak; Liu, Jian; Blaiklock, Peter; Shworak, Nicholas

W.; Bai, Xiaomei; Esko, Jeffrey D.; Cohen, Gary H.; Eisenberg, Roselyn J.;  
**Rosenberg, Robert D.; Spear, Patricia G.**

CS Department of Microbiology-Immunology, Northwestern University Medical  
 School, Chicago, IL, 60611, USA

SO Cell (Cambridge, Massachusetts) (1999), 99(1), 13-22  
 CODEN: CELLB5; ISSN: 0092-8674

PB Cell Press  
DT Journal  
LA English  
CC 14-3 (Mammalian Pathological Biochemistry)  
Section cross-reference(s): 3, 7, 10  
AB **Herpes simplex virus type**  
1 (HSV-1) binds to cells through interactions of viral glycoproteins gB and gC with **heparan sulfate** chains on cell surface proteoglycans. This binding is not sufficient for viral entry, which requires fusion between the viral envelope and cell membrane. Here, the authors show that **heparan sulfate** modified by a subset of the multiple D-glucosaminyl 3-O-sulfotransferase isoforms provides sites for the binding of a third viral glycoprotein, gD, and for initiation of HSV-1 entry. The authors conclude that susceptibility of cells to HSV-1 entry depends on (1) presence of **heparan sulfate** chains to which virus can bind and (2) 3-O-sulfation of specific glucosamine residues in **heparan sulfate** to generate gD-binding sites or the expression of other previously identified gD-binding receptors.  
ST sulfated **heparan sulfate herpes simplex virus 1** entry; glucosaminyl sulfotransferase cDNA sequence mouse  
IT **Sulfation**  
(biol.; **heparan sulfate** 3-O-sulfated by D-glucosaminyl 3-O-sulfotransferases provides sites for binding by glycoprotein gD for **herpes simplex virus 1** entry)  
IT Mouse (Mus musculus)  
Protein sequences  
cDNA sequences  
(cDNA sequence of mouse D-glucosaminyl 3-O-sulfotransferase isoenzyme 3B)  
IT Receptors  
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence); PROC (Process)  
(for glycoprotein gD; **heparan sulfate** 3-O-sulfated by D-glucosaminyl 3-O-sulfotransferases provides sites for binding by glycoprotein gD for **herpes simplex virus 1** entry)  
IT Glycoproteins, specific or class  
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(gD; **heparan sulfate** 3-O-sulfated by D-glucosaminyl 3-O-sulfotransferases provides sites for binding by glycoprotein gD for **herpes simplex virus 1** entry)  
IT **Human herpesvirus 1**  
Molecular association  
(**heparan sulfate** 3-O-sulfated by D-glucosaminyl 3-O-sulfotransferases provides sites for binding by glycoprotein gD for **herpes simplex virus 1** entry)  
IT Proteoglycans, biological studies  
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PROC (Process)  
(heparitin sulfate-contg., 3-O-sulfated; **heparan**

**sulfate 3-O-sulfated by D-glucosaminyl 3-O-sulfotransferases** provides sites for binding by glycoprotein gD for **herpes simplex virus 1** entry)

## IT Infection

(viral; **heparan sulfate 3-O-sulfated by D-glucosaminyl 3-O-sulfotransferases** provides sites for binding by glycoprotein gD for **herpes simplex virus 1** entry)

## IT 251924-96-6

RL: PRP (Properties)

(amino acid sequence; cDNA sequence of mouse **D-glucosaminyl 3-O-sulfotransferase isoenzyme 3B**)

## IT 183257-54-7, Heparan sulfate D

-glucosaminyl 3-O-sulfotransferase

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)

(**heparan sulfate 3-O-sulfated by D-glucosaminyl 3-O-sulfotransferases** provides sites for binding by glycoprotein gD for **herpes simplex virus 1** entry)

## IT 9050-30-0D, Heparan sulfate, 3-O-sulfated

RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PROC (Process)

(**heparan sulfate 3-O-sulfated by D-glucosaminyl 3-O-sulfotransferases** provides sites for binding by glycoprotein gD for **herpes simplex virus 1** entry)

## IT 245809-58-9, GenBank AF168992

RL: PRP (Properties)

(nucleotide sequence; cDNA sequence of mouse **D-glucosaminyl 3-O-sulfotransferase isoenzyme 3B**)

RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD.

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## IT 183257-54-7, Heparan sulfate D

-glucosaminyl 3-O-sulfotransferase

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)

(heparan sulfate 3-O-sulfated by D

-glucosaminyl 3-O-sulfotransferases

provides sites for binding by glycoprotein gD for

herpes simplex virus 1 entry)

RN 183257-54-7 HCAPLUS

CN Sulfotransferase, heparitin 3- (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

## IT 9050-30-0D, Heparan sulfate, 3-O-sulfated

RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PROC (Process)

(heparan sulfate 3-O-sulfated by D

-glucosaminyl 3-O-sulfotransferases

provides sites for binding by glycoprotein gD for

herpes simplex virus 1 entry)

RN 9050-30-0 HCAPLUS

CN Heparan, sulfate (9CI) (CA INDEX NAME)

CM 1

CRN 70226-44-7

CMF Unspecified

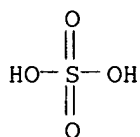
CCI MAN

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

CM 2

CRN 7664-93-9

CMF H2 O4 S



L160 ANSWER 7 OF 11 HCAPLUS COPYRIGHT 2003 ACS

AN 1997:465326 HCAPLUS

DN 127:187154

TI Glycoprotein D of **herpes** simplex virus (**HSV**)

binds directly to HVEM, a member of the tumor necrosis factor receptor superfamily and a mediator of **HSV** entry

AU Whitbeck, J. Charles; Peng, Charline; Lou, Huan; Xu, Ruliang; Willis, Sharon H.; Ponce de Leon, Manuel; Peng, Tao; Nicola, Anthony V.; Montgomery, Rebecca I.; Warner, Morgyn S.; Soulika, Athena M.; Spruce, Lynn A.; Moore, William T.; Lambris, John D.; **Spear, Patricia G.**; Cohen, Gary H.; Eisenberg, Roselyn J.

CS School of Dental Medicine, Center for Oral health Research, School of Veterinary Medicine and School of Medicine, University of Pennsylvania, Philadelphia, PA, 19104, USA

SO Journal of Virology (1997), 71(8), 6083-6093  
CODEN: JOVIAM; ISSN: 0022-538X

PB American Society for Microbiology

DT Journal

LA English

CC 6-3 (General Biochemistry)

Section cross-reference(s): 3, 10, 15

AB Glycoprotein D (**gD**) is a structural component of the **herpes** simplex virus (**HSV**) envelope which is essential for virus entry into host cells. Chinese hamster ovary (CHO-K1) cells are one of the few cell types which are nonpermissive for the entry of many **HSV** strains. However, when these cells are transformed with the gene for the **herpesvirus** entry mediator (HVEM), the resulting cells, CHO-HVEM12, are permissive for many **HSV** strains, such as **HSV-1(KOS)**. By virtue of its four cysteine-rich pseudorepeats, HVEM is a member of the tumor necrosis factor superfamily of proteins. Recombinant forms of **gD** and HVEM, **gD-1(306t)** and HVEM(200t), resp., were used to demonstrate a specific phys. interaction between these two proteins. This interaction was dependent on native **gD** conformation but independent of its N-linked **oligosaccharides**, as expected from previous structure-function studies. Recombinant forms of **gD** derived from **HSV-1(KOS)rid1** and **HSV-1(ANG)** did not bind to HVEM(200t), explaining the inability of these viruses to infect CHO-HVEM12 cells. A variant **gD** protein, **gD-1(.DELTA.290-299t)**, showed enhanced binding to HVEM(200t) relative to the binding of **gD-1(306t)**. Competition studies showed that **gD-1(.DELTA.290-299t)** and **gD-1(306t)** bound to the same region of HVEM(200t), suggesting that the differences in binding to HVEM are due to differences in affinity. These differences were also reflected in the ability of **gD-1(.DELTA.290-299t)** but not **gD-1(306t)** to block **HSV** type 1 infection of CHO-HVEM12 cells. By gel filtration chromatog., the complex between **gD-1(.DELTA.290-299t)** and HVEM(200t) had a mol. mass of 113 kDa and a molar ratio of 1:2. We conclude that HVEM interacts directly with **gD**, suggesting that HVEM is a receptor for virion **gD** and that the interaction between these proteins is a step in **HSV** entry into HVEM-expressing cells.

ST **HSV** glycoprotein D HVEM interaction;

- herpesvirus** entry mediator glycoprotein D interaction
- IT Proteins, specific or class  
 RL: BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); PROC (Process)  
 (HVEM (**herpesvirus** entry mediator); HVEM interacts directly with glycoprotein **gD**, suggesting that HVEM is a receptor for the **herpes** simplex virus **gD**, and interaction between these proteins is a step in **herpes** simplex virus entry)
- IT Glycoproteins, specific or class  
 RL: BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); PROC (Process)  
 (**gD**; HVEM interacts directly with glycoprotein **gD**, suggesting that HVEM is a receptor for the **herpes** simplex virus **gD**, and interaction between these proteins is a step in **herpes** simplex virus entry)
- IT Human **herpesvirus**  
 Molecular cloning  
 (glycoprotein D of **herpes** simplex virus (**HSV**) binds directly to HVEM, a member of the tumor necrosis factor receptor superfamily and a mediator of **HSV** entry)
- IT Tumor necrosis factor receptors  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (glycoprotein D of **herpes** simplex virus (**HSV**) binds directly to HVEM, a member of the tumor necrosis factor receptor superfamily and a mediator of **HSV** entry)
- L160 ANSWER 8 OF 11 HCAPLUS COPYRIGHT 2003 ACS  
 AN 1995:361806 HCAPLUS  
 DN 122:156187  
 TI Identification of structural features of heparin required for inhibition of **herpes simplex virus type 1** binding  
 AU Herold, Betsy C.; Gerber, Susan Ilene; Polonsky, Tamar; Belval, Brian J.; Shaklee, Patrick N.; Holme, Kevin  
 CS Univ. of Chicago, Section of Pediatric Infectious Diseases and Committee on Virology, Chicago, IL, 60637-1470, USA  
 SO Virology (1995), 206(2), 1108-16  
 CODEN: VIRLAX; ISSN: 0042-6822  
 PB Academic  
 DT Journal  
 LA English  
 CC 10-6 (Microbial, Algal, and Fungal Biochemistry)  
 AB Binding of **HSV-1** to cells is mediated by interactions of virion glycoproteins gC and/or gB with **heparan sulfate** (HS) glycosaminoglycans on cell surface proteoglycans. HS and the related glycosaminoglycan, heparin, comprise a family of heterogeneous carbohydrates composed of long, unbranched polysaccharides modified, for example, by sulfations and acetylations. To define the specific features of HS important for viral binding, we took advantage of the structural similarities between heparin and cell surface HS and compared the ability of chem. modified heparin compds. to inhibit the binding of viral particles to the cell surface and subsequent plaque formation. Because binding presumably involves multiple, complex interactions between known heparin-binding glycoproteins, gC and gB, and cell surface HS, we compared the effects of modified heparin compds. on the binding and subsequent plaque formation of wild-type and gC-neg. strains of **HSV-1** and, in select cases, the binding of gB-neg. virus to cells. We identified specific structural features of heparin essential for the inhibition of viral binding. For example, both N-sulfation and 6-O-sulfation must be important determinants since

desulfation of heparin at these sites abolished or decreased the antiviral activity of heparin. Moreover, we found that the antiviral activity of heparin was independent of its anticoagulant activity. Carboxyl-reduced and 2-,3-O desulfated heparin selectively inhibited binding of gC-pos. viruses (wild-type or a g-neg. strain) to cells, but had little or no inhibitory effect on binding and subsequent plaque formation for a gC-deletion virus. These results suggest that gC and gB interact with different structural features of HS.

- ST **herpes simplex virus binding heparin structure**
- IT Molecular structure-biological activity relationship  
(**herpes simplex virus-binding**; of heparin)
- IT **Sulfation**  
(structural features of heparin required for inhibition of  
**herpes simplex virus type 1** binding in relation to)
- IT Glycoproteins, specific or class  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(gB, structural features of heparin required for binding to  
**herpes simplex virus type 1** glycoprotein gB)
- IT Glycoproteins, specific or class  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(gC, structural features of heparin required for binding to  
**herpes simplex virus type 1** glycoprotein gC)
- IT **Virus, animal**  
(**herpes simplex 1**, structural features of heparin required for inhibition of **herpes simplex virus type 1** binding)
- IT 9005-49-6, Heparin sulfate, biological studies  
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)  
(structural features of heparin required for inhibition of  
**herpes simplex virus type 1** binding)

L160 ANSWER 9 OF 11 HCAPLUS COPYRIGHT 2003 ACS

AN 1983:503433 HCAPLUS

DN 99:103433

TI Characterization of a **herpes simplex virus type 2**  
75,000-molecular-weight glycoprotein antigenically related to  
**herpes simplex virus type 1**  
glycoprotein C

AU Zezulak, Kathleen M.; Spear, Patricia G.

CS Dep. Microbiol., Univ. Chicago, Chicago, IL, 60637, USA

SO Journal of Virology (1983), 47(3), 553-62

CODEN: JOVIAM; ISSN: 0022-538X

DT Journal

LA English

CC 15-2 (Immunochemistry)

Section cross-reference(s): 10

AB Evidence is presented that the **herpes simplex virus type 2** glycoprotein previously designated gF is antigenically related to **herpes simplex virus type 1** glycoprotein (gC-1). An antiserum prepd. against type 1 virion envelope proteins immunopptd. gF of type 2 (gF-2), and competition expts. revealed that the anti-gC-1 component of the antiserum was responsible for the anti-gF-2 cross-reactivity. An antiserum prepd. against fully denatured purified gF-2, however, and 3 anti-gF-2 monoclonal antibodies failed to ppt. any type 1 antigen, indicating that the extent of cross-reactivity

between gC-1 and gF-2 may be limited. Several aspects of gF-2 synthesis and processing were investigated: Use of the enzymes endo-.beta.-N-acetylglucosaminidase H and .alpha.-D-N-acetylgalactosaminyl **oligosaccharidase** revealed that the fully processed form of gF-2 [about 75,000 (75K) apparent mol. wt.] had both complex-type N-linked and O-linked **oligosaccharides**, whereas newly synthesized forms (67K and 69K) had only high-mannose N-linked **oligosaccharides**. These last 2 forms were both reduced in size to 54K by treatment with endo-.beta.-N-acetylglucosaminidase H and therefore appear to differ only in the no. of N-linked chains. Neutralization tests and radioiodination expts. revealed that gF-2 is exposed on the surfaces of virions and that the 75K form of gF-2 is exposed on cell surfaces. The similarities and differences of gF-2 and gC-1 are discussed in light of recent mapping results which suggest collinearity of their resp. genes.

ST **herpes virus glycoprotein antigenicity**

IT Antigenes

RL: BIOL (Biological study)

(**herpes simplex virus glycoproteins C and F** as, similarities of, of human)

IT Glycoproteins

RL: BIOL (Biological study)

(C, of **herpes simplex virus type**

1, type 2 glycoprotein F antigenic similarity to, of human)

IT Glycoproteins

RL: BIOL (Biological study)

(F, of **herpes simplex virus type 2**, formation of and type 2 glycoprotein F antigenic similarity to, of human)

IT **Virus, animal**

(**herpes simplex 1**, glycoprotein C of,

type 2 glycoprotein F antigenic similarity to, of human)

IT **Virus, animal**

(**herpes simplex 2**, glycoprotein F of, type 1 glycoprotein C antigenic similarity to, of human)

L160 ANSWER 10 OF 11 HCAPLUS COPYRIGHT 2003 ACS

AN 1983:156693 HCAPLUS

DN 98:156693

TI O-linked **oligosaccharides** are acquired by **herpes simplex virus glycoproteins** in the Golgi apparatus

AU Johnson, David C.; Spear, Patricia G.

CS Dep. Microbiol., Univ. Chicago, Chicago, IL, 60637, USA

SO Cell (Cambridge, MA, United States) (1983), 32(3), 987-97

CODEN: CELLB5; ISSN: 0092-8674

DT Journal

LA English

CC 6-3 (General Biochemistry)

AB The O-linked **oligosaccharides** on mature forms of **herpes simplex virus type 1 (HSV1**

) glycoproteins were characterized and found to account largely for the lower electrophoretic mobilities of these forms relative to the mobilities of immature forms. Other posttranslational modifications of **HSV1** glycoproteins (designated gB, gC, gD, and gE) were related temporally to the discrete shifts in electrophoretic mobilities that signal acquisition of the O-linked **oligosaccharides**. Fatty acid acylation (principally of gE) could be detected just prior to the shifts, whereas conversion of high-mannose-type N-linked **oligosaccharides** to the complex type occurred coincident with the shifts. The addn. of O-linked **oligosaccharides** did not occur in cells treated with the ionophore monensin or in a ricin-resistant cell line defective in the processing of N-linked **oligosaccharides**. Evidently, extension of O-linked **oligosaccharide** chains on **HSV1** glycoproteins, and probably also attachment of the first O-linked sugars, occurs as a late posttranslational modification in the Golgi app.



ST glycoprotein **oligosaccharide herpes** simplex virus;  
Golgi app glycoprotein modification; fatty acid acylation glycoprotein  
IT Fatty acids, biological studies  
RL: BIOL (Biological study)  
(glycoprotein of **herpes** simplex virus acylation by, O-linked  
**oligosaccharides** in relation to)  
IT Golgi apparatus  
(glycoproteins of **herpes** simplex virus processing by O-linked  
**oligosaccharides** in)  
IT Glycoproteins  
RL: PROC (Process)  
(O-linked **oligosaccharide** processing of, of **herpes**  
simplex virus)  
IT **Oligosaccharides**  
RL: BIOL (Biological study)  
(O-linked, glycoproteins of **herpes** simplex virus attachment  
of)  
IT **Virus, animal**  
(**herpes simplex 1**, glycoproteins of,  
O-linked **oligosaccharide** processing of)

L160 ANSWER 11 OF 11 HCAPLUS COPYRIGHT 2003 ACS

AN 1981:44880 HCAPLUS

DN 94:44880

TI Evidence for a 3-O-sulfated D-glucosamine residue in the  
antithrombin-binding sequence of heparin

AU Lindahl, Ulf; Baeckstroem, Gudrun; Thunberg, Lennart; Leder, Irwin G.

CS Biomed. Cent., Swed. Univ. Agric. Sci., Uppsala, S-751 23, Swed.

SO Proceedings of the National Academy of Sciences of the United States of  
America (1980), 77(11), 6551-5

CODEN: PNASA6; ISSN: 0027-8424

DT Journal

LA English

CC 13-5 (Mammalian Biochemistry)

Section cross-reference(s): 6

AB An octasaccharide with high affinity for antithrombin was isolated after  
partial deaminative cleavage of heparin with HNO<sub>2</sub>. After conversion of  
the 2,5-anhydro-D-mannose end group to anhydro[1-3H]mannitol,  
labeled pentasaccharide was released from the octasaccharide by  
periodate-alkali treatment. Incubation of the pentasaccharide with a  
3-O-sulfatase from human urine resulted in desulfation, suggesting the  
occurrence of a 3-sulfate group on the terminal glucosamine residue. The  
same glucosamine residue was recovered as a 2,5-anhydro[1-3H]mannitol  
deriv. by a procedure involving deamination of the octasaccharide with  
HNO<sub>2</sub>, redn. of the products with NaBH<sub>4</sub>, isolated of 3H-labeled  
tetrasaccharide by gel chromatog., and release of the labeled end group by  
periodate-alkali treatment. Paper electrophoresis indicated disulfated  
anhydro[3H]mannitol, presumably sulfated at C3 and C6, as a major  
component, along with smaller amts. of monosulfated (presumably  
3-sulfated) anhydro[3H]mannitol. Similar treatment of an analogous  
tetrasaccharide derived from heparin with low affinity for antithrombin  
failed to produce any disulfated anhydromannitol. Evidently, 3-sulfated  
glucosamine is a unique component of high-affinity heparin, located at a  
specific position in the antithrombin-binding sequence of the mol.

ST antithrombin heparin binding glucosamine sulfate

IT 9005-49-6, biological studies

RL: BIOL (Biological study)

(antithrombin binding by, sulfated glucosamine residue in)

IT 9000-94-6

RL: BIOL (Biological study)

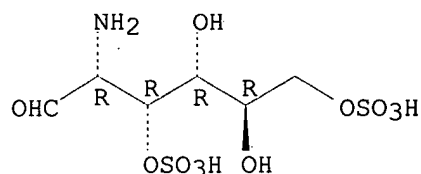
(heparin binding by, sulfated glucosamine residue in)

IT 76330-20-6 76330-21-7

RL: BIOL (Biological study)

(of heparin, antithrombin binding in relation to)  
 IT 76330-21-7  
 RL: BIOL (Biological study)  
 (of heparin, antithrombin binding in relation to)  
 RN 76330-21-7 HCAPLUS  
 CN D-Glucose, 2-amino-2-deoxy-, 3,6-bis(hydrogen sulfate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> d all hitstr tot 1155

L155 ANSWER 1 OF 10 HCAPLUS COPYRIGHT 2003 ACS  
 AN 1994:524657 HCAPLUS  
 DN 121:124657  
 TI Neomycin inhibits glycoprotein C (gC)-dependent binding of **herpes simplex virus type 1** to cells and also inhibits postbinding events in entry  
 AU Herold, Betsy C.; Spear, Patricia G.  
 CS Section of Pediatric Infectious Diseases, Univ. Chicago, Chicago, IL, 60637-1470, USA  
 SO Virology (1994), 203(1), 166-71  
 CODEN: VIRLAX; ISSN: 0042-6822  
 DT Journal  
 LA English  
 CC 1-5 (Pharmacology)  
 AB Previous studies have identified requirements for the binding of **herpes simplex virus type 1** (HSV-1) to cells, including the presence of particular glycoproteins in the virion envelope (gC or gB) and the presence of particular glycosaminoglycan chains (principally **heparan sulfate**) on cell surface proteoglycans. The authors show here that neomycin, a known inhibitor of HSV infection, blocked early events in HSV infection by two mechanisms: partial inhibition of the gC-dependent binding of virions, but not the gB-dependent binding, and inhibition of events that occurred after the binding of virus to cells. Near-maximal (but incomplete) inhibition of virus binding occurred at low concns. of neomycin (1 mM) for wild-type and gB-neg. virions only. Neomycin also inhibited the binding of isolated gC to cells at a similar concn. Concns. of neomycin as high as 50 mM had little or no effect on the binding of gC-neg. virions to cells. Nevertheless, neomycin significantly inhibited infection by both wild-type and gC-neg. virions, at concns. greater than 10 mM, indicating that the inhibition at higher doses was not due to effects on virus binding. The effects of neomycin on virus binding suggest that gC (but not gB) and neomycin compete for binding to similar structural features of cell surface **heparan sulfate**.  
 ST **herpes** virus glycoprotein C binding neomycin; virucide neomycin **herpes** glycoprotein binding cell  
 IT Virucides and Virustats  
 (neomycin, glycoprotein C-dependent binding of **herpes simplex virus type 1** to cells inhibition by)

- IT Glycoproteins, specific or class  
RL: BIOL (Biological study)  
(B, of **herpes simplex virus type 1**, cell binding dependent on, neomycin effect on)
- IT Glycoproteins, specific or class  
RL: BIOL (Biological study)  
(gC, of **herpes simplex virus type 1**, cell binding dependent on, neomycin inhibition of)
- IT **Virus, animal**  
(**herpes simplex 1**, glycoprotein C-dependent binding of, to cells, neomycin inhibition of)
- IT 1404-04-2, Neomycin  
RL: BIOL (Biological study)  
(glycoprotein C-dependent binding of **herpes simplex virus type 1** to cells inhibition by)
- L155 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2003 ACS  
AN 1994:432256 HCAPLUS  
DN 121:32256  
TI Glycoprotein C-independent binding of **herpes simplex virus** to cells requires cell surface **heparan sulfate** and glycoprotein B  
AU Herold, Betsy C.; Visalli, Robert J.; Susmarski, Nanette; Brandt, Curtis R.; **Spear, Patricia G.**  
CS Dep. Microbiol.-Immunol., Northwestern Univ. Med. Dental Schools, Chicago, IL, 60611, USA  
SO Journal of General Virology (1994), 75(6), 1211-22  
CODEN: JGVIAI; ISSN: 0022-1317  
DT Journal  
LA English  
CC 14-3 (Mammalian Pathological Biochemistry)  
AB Previous studies have shown that the initial interaction of **herpes simplex virus (HSV)** with cells is binding to **heparan sulfate** and that **HSV-1** glycoprotein C (gC) is principally responsible for this binding. Although gC-neg. viral mutants are impaired for binding and entry, they retain significant infectivity. The purpose of the studies reported here was to explore the requirements for infectivity of gC-neg. **HSV-1** mutants. The authors found that absence or alteration of cell surface **heparan sulfate** significantly reduced the binding of gC-neg. mutant virus and rendered cells resistant to infection, as shown previously for the wild-type virus. The authors isolated a recombinant double-mutated **HSV** strain that produces virions devoid of both of the known heparin-binding glycoproteins, gB and gC. The drastically impaired binding of these mutant virions to cells, relative to gC-neg. and wild-type virions, indicates that gB mediates the binding of gC-neg. virions to cells. Thus at least two **HSV** glycoproteins can independently mediate the binding of **HSV** to cell surface **heparan sulfate** to start the process of viral entry into cells.
- ST glycoprotein C B **HSV** cell infection  
IT Infection  
(with **HSV-1**, cell surface **heparan sulfate** and glycoprotein B in binding of glycoprotein C-neg mutants in relation to)
- IT Glycoproteins, specific or class  
RL: BIOL (Biological study)  
(B, **heparan sulfate** and, in **HSV-1** cell surface binding and infectivity)
- IT Glycoproteins, specific or class  
RL: BIOL (Biological study)  
(C, infectivity of **HSV-1** mutants neg. for)

L155 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2003 ACS

AN 1994:103708 HCAPLUS

DN 120:103708

TI **Herpesvirus**-induced cell fusion that is dependent on cell surface **heparan sulfate** or soluble heparin

AU Shieh, Mei Tsu; **Spear, Patricia G.**

CS Med. Sch., Northwestern Univ., Chicago, IL, 60611, USA

SO Journal of Virology (1994), 68(2), 1224-8

CODEN: JOVIAM; ISSN: 0022-538X

DT Journal

LA English

CC 14-3 (Mammalian Pathological Biochemistry)

Section cross-reference(s): 10

AB The entry of enveloped viruses into animal cells and the cell-to-cell spread of infection via cell fusion require the membrane-fusing activity of viral glycoproteins. This activity can be dependent on variable cell factors or triggered by environmental factors. Here the authors show that cell fusion induced by **herpes** simplex virus glycoproteins is dependent on the presence of cell surface glycosaminoglycans, principally **heparan sulfate**, or on the addn. of heparin to the medium. The role of the glycosaminoglycan is probably to alter the conformation of a viral heparin-binding glycoprotein required for the fusion.

ST **herpesvirus** adhesion heparan glycosaminoglycan infection

IT Glycosaminoglycans, biological studies

RL: BIOL (Biological study)

(**HSV-1** fusion mediation by, of infected cell)

IT Infection

(by **HSV-1**, cell glycosaminoglycan mediation of binding of)

IT Adhesion

(bio-, of **HSV-1** to mammalian cells, glycosaminoglycan mediation of)

IT **Virus, animal**

(**herpes simplex 1**, cell glycosaminoglycan mediation of binding of)

IT 70226-44-7, Heparan

RL: BIOL (Biological study)

(**HSV-1** fusion to infected cells mediation by)

L155 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2003 ACS

AN 1993:512994 HCAPLUS

DN 119:112994

TI Entry of **alphaherpesviruses** into cells

AU **Spear, P. G.**

CS Med. Sch., Northwestern Univ., Chicago, IL, 60611, USA

SO Seminars in Virology (1993), 4(3), 167-80

CODEN: SEVIEL; ISSN: 1044-5773

DT Journal; General Review

LA English

CC 10-0 (Microbial, Algal, and Fungal Biochemistry)

Section cross-reference(s): 14

AB A review with 103 refs. Studies on four **alphaherpesviruses** (**herpes simplex virus types 1**

and 2, pseudorabies virus and bovine **herpesvirus 1**)

have revealed some common features of their entry into cells. The pathway of entry can be by fusion of the virion envelope with the cell plasma membrane. Receptors for binding and entry include **heparan sulfate** moieties of cell surface proteoglycans and other as yet unidentified cell surface components. Related glycoproteins specified by each of the four viruses mediate the binding of virus to **heparan sulfate** and subsequent mol. interactions leading to the penetration of virus into the cell.

ST **alphaherpesvirus** entry cell review  
IT **Virus, animal**  
    (**herpes simplex 1**, infection with, cell entry mechanism of)  
IT **Virus, animal**  
    (**herpes simplex 2**, infection with, cell entry mechanism of)  
IT **Virus, animal**  
    (infectious bovine rhinotracheitis, infection with, cell entry mechanism of)  
IT **Virus, animal**  
    (pseudorabies, infection with, cell entry mechanism of)

L155 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2003 ACS  
AN 1993:210239 HCAPLUS  
DN 118:210239  
TI Cell surface receptors required for **herpes simplex virus** infection include **heparan sulfate** glycosaminoglycans  
AU **Spear, Patricia G.**; Shieh, Mei Tsu; Herold, Betsy C.; WuDunn, Darrell  
CS Med. Sch., Northwestern Univ., Chicago, IL, 60611, USA  
SO Microb. Adhes. Invasion, [Proc. Symp.] (1992), Meeting Date 1990, 43-57. Editor(s): Hook, Magnus; Switalski, Lech. Publisher: Springer, New York, N. Y.  
CODEN: 58SJAY  
DT Conference; General Review  
LA English  
CC 14-0 (Mammalian Pathological Biochemistry)  
Section cross-reference(s): 10  
AB A review with 49 refs. There are a no. of viruses for which the only known specific interaction with the cell surface is binding to a carbohydrate moiety of a cell surface glycoprotein or glycolipid. In our view, **HSV** belongs in this category, at least for the present. The possibility exists, for any of these viruses, that the initial specific interaction with a carbohydrate leads to other specific interactions with proteins, lipids, etc. Because most of these viruses have broad host ranges, any specific receptors required must be highly conserved and broadly distributed. The interaction of **HSV** with **heparan sulfate** and heparin-like mols. could have functional significance in several ways. First, the binding of **HSV** to cell surface **heparan sulfate** serves to conc. virus on the cell surface. Second, inasmuch as many heparin-binding proteins are altered structurally and functionally by their interactions with heparin, the possibility exists that the binding of **HSV** glycoproteins to heparin sulfate activates functions required for viral penetration. Third, because both heparin and heparin-binding proteins can inhibit **HSV** infection and because structural tissue elements such as basement membranes are rich in **heparan sulfate** proteoglycans, the possibility exists that interactions of virus with any of these non-cell-assocd. mols. may serve to limit the spread of **HSV** infection, explaining perhaps the localized nature of most **HSV** infections.

ST **herpes simplex virus** cell receptor review; **heparan sulfate herpes virus** receptor review  
IT Cell membrane  
    (**heparan sulfate** as **herpes simplex virus** receptor of)  
IT Receptors  
    RL: BIOL (Biological study)  
        (**herpes simplex virus**, **heparan sulfate** as, for **herpes simplex virus**, in host cell surface)  
IT 9050-30-0  
    RL: BIOL (Biological study)  
        (as cell surface receptor for **herpes simplex virus**)

IT 9050-30-0  
 RL: BIOL (Biological study)  
 (as cell surface receptor for **herpes** simplex virus)  
 RN 9050-30-0 HCAPLUS  
 CN Heparan, sulfate (9CI) (CA INDEX NAME)

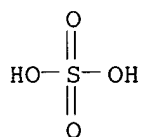
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CRN 70226-44-7  
 CMF Unspecified  
 CCI MAN

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

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CRN 7664-93-9  
 CMF H2 O4 S



L155 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2003 ACS  
 AN 1993:166066 HCAPLUS  
 DN 118:166066  
 TI **Heparan sulfate** glycosaminoglycans as primary cell  
 surface receptors for **herpes** simplex virus  
 AU **Spear, Patricia G.**; Shieh, Mei Tsu; Herold, Betsy C.; WuDunn,  
 Darrell; Koshy, Thomas I.  
 CS Med. Sch., Northwestern Univ., Chicago, IL, 60611, USA  
 SO Advances in Experimental Medicine and Biology (1992),  
 313(Heparin Relat. Polysaccharides), 341-53  
 CODEN: AEMBAP; ISSN: 0065-2598  
 DT Journal; General Review  
 LA English  
 CC 14-0 (Mammalian Pathological Biochemistry)  
 AB A review, with 63 refs., which to summarizes the evidence that  
**heparan sulfate** moieties of proteoglycans serve as cell  
 surface receptors for **herpes** simplex virus (HSV) and  
 describes the heparin-binding viral glycoproteins that mediate the binding  
 of virus to cells. These topics are discussed in the context of the mol.  
 interactions required for entry of HSV into cells and, also, the  
 pathol. of HSV infections.  
 ST review **heparan sulfate** glycosaminoglycan  
**herpes** virus  
 IT Glycosaminoglycans, biological studies  
 RL: BIOL (Biological study)  
 (heparitin sulfate-contg., as **herpes** simplex virus receptors,  
 on human cell surfaces)  
 IT Virus, animal  
 (**herpes** simplex, receptors for, **heparan**  
**sulfate** glycosaminoglycans as, on human cell surfaces)  
 IT Receptors  
 RL: BIOL (Biological study)  
 (**herpes** simplex virus, **heparan sulfate**  
 glycosaminoglycan as, on human cell surfaces)

L155 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2003 ACS

AN 1992:103565 HCAPLUS

DN 116:103565

TI Cell surface receptors for **herpes** simplex virus are  
**heparan sulfate** proteoglycans

AU Shieh, Mei Tsu; WuDunn, Darrell; Montgomery, Rebecca I.; Esko, Jeffrey D.;  
**Spear, Patricia G.**

CS Med. Sch., Northwestern Univ., Chicago, IL, 60611, USA

SO Journal of Cell Biology (1992), 116(5), 1273-81

CODEN: JCLBA3; ISSN: 0021-9525

DT Journal

LA English

CC 14-3 (Mammalian Pathological Biochemistry)

Section cross-reference(s): 10

AB The role of cell surface **heparan sulfate** in  
**herpes** simplex virus (HSV) infection was investigated  
using CHO cell mutants defective in various aspects of glycosaminoglycan  
synthesis. Binding of radiolabeled virus to the cells and infection were  
assessed in mutant and wild-type cells. Virus bound efficiently to  
wild-type cells and initiated an abortive infection in which  
immediate-early or .alpha. viral genes were expressed, despite limited  
prodn. of late viral proteins and progeny virus. Binding of virus to  
**heparan sulfate**-deficient mutant cells was severely  
impaired and mutant cells were resistant to HSV infection.  
Intermediate levels of binding and infection were obsd. for a CHO cell  
mutant that produced undersulfated **heparan sulfate**.  
These results show that **heparan sulfate** moieties of  
cell surface proteoglycans serve as receptors for HSV.

ST **herpes** simplex virus receptor **heparan sulfate**

IT Cell membrane

(**heparan sulfate** proteoglycans as **herpes**  
simplex virus receptors at surface of)

IT Proteoglycans, biological studies

RL: BIOL (Biological study)

(heparitin sulfate-contg., as **herpes** simplex virus receptors  
at cell surface)

IT Virus, animal

(**herpes** simplex, receptors for, **heparan**  
**sulfate** proteoglycans of cell surface as)

IT Receptors

RL: BIOL (Biological study)

(**herpes** simplex virus, **heparan sulfate**  
proteoglycans of cell surface as)

IT 9050-30-0, **Heparan sulfate**

RL: BIOL (Biological study)

(as **herpes** simplex virus receptors at cell surface)

IT 9050-30-0, **Heparan sulfate**

RL: BIOL (Biological study)

(as **herpes** simplex virus receptors at cell surface)

RN 9050-30-0 HCAPLUS

CN Heparan, sulfate (9CI) (CA INDEX NAME)

CM 1

CRN 70226-44-7

CMF Unspecified

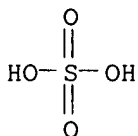
CCI MAN

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

CM 2

CRN 7664-93-9

CMF H2 O4 S



L155 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2003 ACS

AN 1991:118396 HCAPLUS

DN 114:118396

TI Glycoprotein C of **herpes simplex virus****type 1** plays a principal role in the adsorption of virus to cells and in infectivityAU Herold, Betsy C.; WuDunn, Darrell; Soltys, Nanette; **Spear, Patricia G.**

CS Med. Sch., Northwestern Univ., Chicago, IL, 60611, USA

SO Journal of Virology (1991), 65(3), 1090-8

CODEN: JOVIAM; ISSN: 0022-538X

DT Journal

LA English

CC 10-6 (Microbial Biochemistry)

AB The **herpes simplex virus** glycoprotein that mediates the adsorption of virions to cells was identified. Because **heparan sulfate** moieties of cell surface proteoglycans serve as the receptors for **herpes simplex virus** adsorption, viral glycoprotein binding to heparin-Sepharose was studied in affinity chromatog. expts. Two glycoproteins, gB and gC, bound to heparin-Sepharose and could be eluted with sol. heparin. In order to det. whether virions devoid of gC or gB were impaired for adsorption, the binding of wild-type and mutant virions to cells was quantitated. At equiv. input concns. of purified virions, significantly fewer gC-neg. virions bound to cells than did wild-type or gB-neg. virions. In addn., the gC-neg. virions that bound to cells showed a significant delay in penetration compared with wild-type virus. The impairments in adsorption and penetration of the gC-neg. virions can account for their reduced PFU/particle ratios, which were 5-10% that of wild-type virions, depending on the host cell. Although gC is dispensable for replication of **herpes simplex** in cell culture, it clearly facilitates virion adsorption and enhances infectivity by about a factor of 10.

ST glycoprotein C **herpes simplex virus** adsorption

IT Microbial virulence

(of **herpes simplex virus type**  
1, glycoprotein C in)

IT Adsorption

(of **herpes simplex virus type**  
1, to host cells, glycoprotein C in)

IT Glycoproteins, specific or class

RL: BIOL (Biological study)

(gC, of **herpes simplex virus 1**,  
in adsorption and infectivity of virus)

IT **Virus, animal**

(**herpes simplex 1**, glycoprotein C of, in  
adsorption of virus to cells and infectivity)

L155 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2003 ACS

AN 1989:55215 HCAPLUS

DN 110:55215

TI Initial interaction of **herpes simplex virus** with cells is  
binding to **heparan sulfate**

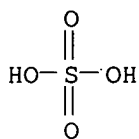


AU WuDunn, Darrell; Spear, Patricia G.  
CS Dep. Mol. Genet. Cell Biol., Univ. Chicago, Chicago, IL, 60637, USA  
SO Journal of Virology (1989), 63(1), 52-8  
CODEN: JOVIAM; ISSN: 0022-538X  
DT Journal  
LA English  
CC 14-3 (Mammalian Pathological Biochemistry)  
Section cross-reference(s): 10  
AB It was shown that cell surface **heparan sulfate** serves as the initial receptor for both serotypes of **herpes simplex virus (HSV)**. It was also found that virions could bind to heparin, a related glycosaminoglycan, and that heparin blocked virus adsorption. Agents known to bind to cell surface **heparan sulfate** blocked viral adsorption and infection. Enzymic digestion of cell surface **heparan sulfate** but not of dermatan sulfate or chondroitin sulfate concomitantly reduced the binding of virus to the cells and rendered the cells resistant to infection. Although cell surface **heparan sulfate** was required for infection by **HSV** types 1 and 2, the two serotypes may bind to **heparan sulfate** with different affinities or may recognize different structural features of **heparan sulfate**. Consistent with their broad host ranges, the two **HSV** serotypes use as primary receptors ubiquitous cell surface components known to participate in interactions with the extracellular matrix and with other cell surfaces.  
ST **heparan sulfate** host **herpes** virus receptor  
IT Receptors  
RL: BIOL (Biological study)  
(for **herpes simplex virus**, **heparan sulfate** of host cell surface as)  
IT Cell membrane  
(**heparan sulfate** of, of host cell as **herpes simplex virus** receptor)  
IT **Virus, animal**  
(**herpes simplex 1**, **heparan sulfate** of host cell surface as receptor for)  
IT **Virus, animal**  
(**herpes simplex 2**, **heparan sulfate** of host cell surface as receptor for)  
IT **9050-30-0, Heparan sulfate**  
RL: BIOL (Biological study)  
(of animal cell membrane, as **herpes simplex virus** receptor)  
IT **9050-30-0, Heparan sulfate**  
RL: BIOL (Biological study)  
(of animal cell membrane, as **herpes simplex virus** receptor).  
RN 9050-30-0 HCAPLUS  
CN Heparan, sulfate (9CI) (CA INDEX NAME)  
CM 1  
CRN 70226-44-7  
CMF Unspecified  
CCI MAN

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

CM 2

CRN 7664-93-9  
CMF H2 O4 S



L155 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2003 ACS  
 AN 1986:605876 HCAPLUS  
 DN 105:205876  
 TI Oligomerization of **herpes** simplex virus glycoprotein B  
 AU Claesson-Welsh, L.; **Spear, Patricia G.**  
 CS Dep. Mol. Genet. Cell Biol. Committee Virol., Univ. Chicago, Chicago, IL, 60637, USA  
 SO Journal of Virology (1986), 60(2), 803-6  
 CODEN: JOVIAM; ISSN: 0022-538X  
 DT Journal  
 LA English  
 CC 10-1 (Microbial Biochemistry)  
 AB Glycoprotein B (gB) specified by **herpes** simplex virus was extd. from virions or infected cells in the form of detergent-stable, heat-dissociable oligomers. The compn. of the oligomers and requirements for their formation were investigated. The faster-migrating forms of the oligomers are homodimers of gB. Dimerization occurred within minutes of polypeptide synthesis and did not depend on glycosylation, the expression of other viral proteins, or virion morphogenesis. The multiple, electrophoretically distinct forms of gB dimers differed in extent or rate of N-linked **oligosaccharide** processing and also had other differences that influence electrophoretic mobility.  
 ST **herpes** simplex virus glycoprotein B oligomerization  
 IT **Oligosaccharides**  
 RL: PROC (Process)  
 (of **herpes** simplex virus glycoprotein B oligomers, variable processing of)  
 IT Glycoproteins  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (gB, oligomerization of, of **herpes** simplex virus)  
 IT Virus, animal  
 (herpes simplex, glycoprotein B of, oligomerization of)  
 IT Polymerization  
 (oligomerization, of glycoprotein B of **herpes** simplex virus)

=> sel hit rn 1160  
 E1 THROUGH E4 ASSIGNED

=> fil reg  
 FILE 'REGISTRY' ENTERED AT 16:50:00 ON 06 JUL 2003  
 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
 PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
 COPYRIGHT (C) 2003 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 4 JUL 2003 HIGHEST RN 542812-68-0  
 DICTIONARY FILE UPDATES: 4 JUL 2003 HIGHEST RN 542812-68-0

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003.

Please note that search-term pricing does apply when

conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:

<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=> sel-e4

1 9050-30-0/BI  
 (9050-30-0/RN)  
 1 183257-54-7/BI  
 (183257-54-7/RN)  
 1 328085-46-7/BI  
 (328085-46-7/RN)  
 1 76330-21-7/BI  
 (76330-21-7/RN)

L161 4 (9050-30-0/BI OR 183257-54-7/BI OR 328085-46-7/BI OR 76330-21-7/BI)

=> d ide can tot

L161 ANSWER 1 OF 4 REGISTRY COPYRIGHT 2003 ACS

RN **328085-46-7** REGISTRY

CN D-Glucose, 2-amino-2-deoxy-4-O-(2-O-sulfo-.beta.-L-idopyranuronosyl)-, 3,6-bis(hydrogen sulfate) (9CI) (CA INDEX NAME)

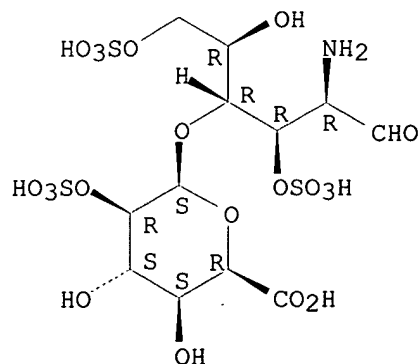
FS STEREOSEARCH

MF C12 H21 N O20 S3

SR CA

LC STN Files: CA, CAPLUS

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1957 TO DATE)  
 1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 134:212717

L161 ANSWER 2 OF 4 REGISTRY COPYRIGHT 2003 ACS

RN **183257-54-7** REGISTRY

CN Sulfotransferase, heparitin 3- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN E.C. 2.8.2.23

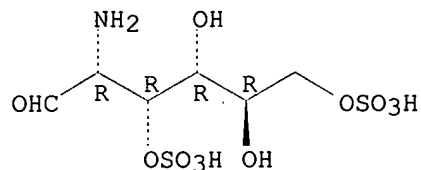
CN Heparan sulfate 3-O-sulfotransferase  
CN Heparan sulfate 3-sulfotransferase  
CN Heparan sulfate D-glucosaminyl 3-O-sulfotransferase  
CN Heparitin 3-sulfotransferase  
MF Unspecified  
CI MAN  
SR CA  
LC STN Files: BIOSIS, CA, CAPLUS, TOXCENTER

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*  
28 REFERENCES IN FILE CA (1957 TO DATE)  
28 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 138:366987  
REFERENCE 2: 138:335272  
REFERENCE 3: 138:300153  
REFERENCE 4: 138:217216  
REFERENCE 5: 138:102854  
REFERENCE 6: 137:380005  
REFERENCE 7: 137:346197  
REFERENCE 8: 137:346196  
REFERENCE 9: 137:306632  
REFERENCE 10: 137:243160

L161 ANSWER 3 OF 4 REGISTRY COPYRIGHT 2003 ACS  
RN 76330-21-7 REGISTRY  
CN D-Glucose, 2-amino-2-deoxy-, 3,6-bis(hydrogen sulfate) (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C6 H13 N O11 S2  
CI COM  
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

5 REFERENCES IN FILE CA (1957 TO DATE)  
5 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 138:198610  
REFERENCE 2: 138:198609  
REFERENCE 3: 137:299942

REFERENCE 4: 134:212717

REFERENCE 5: 94:44880

L161 ANSWER 4 OF 4 REGISTRY COPYRIGHT 2003 ACS

RN 9050-30-0 REGISTRY

CN Heparan, sulfate (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Heparitin sulfate (8CI)

OTHER NAMES:

CN Alpha-Idosane

CN Heparan N-sulfate

CN Heparan sulphate

CN Heparatan sulfate

CN Heparitin

CN Heparitin monosulfate

CN HHS 5

CN N-Acetylheparan sulfate

CN Suleparoid

CN Tavidan

DR 12751-16-5, 11078-25-4, 11097-05-5, 11129-40-1, 29188-70-3

MF H2 O4 S . x Unspecified

CI COM

LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO,  
CA, CABA, CANCERLIT, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CIN, CSCHEM,  
DDFU, DRUGU, DRUGUPDATES, EMBASE, IPA, MEDLINE, PROMT, RTECS\*,  
TOXCENTER, USPAT2, USPATFULL

(\*File contains numerically searchable property data)

Other Sources: EINECS\*\*

(\*\*Enter CHEMLIST File for up-to-date regulatory information)

CM 1

CRN 70226-44-7

CMF Unspecified

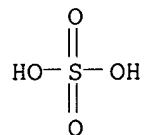
CCI MAN

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

CM 2

CRN 7664-93-9

CMF H2 O4 S



4242 REFERENCES IN FILE CA (1957 TO DATE)

244 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

4250 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 139:26657

REFERENCE 2: 139:19986

REFERENCE 3: 139:19731

REFERENCE 4: 139:17099  
REFERENCE 5: 139:5397  
REFERENCE 6: 139:4604  
REFERENCE 7: 139:4186  
REFERENCE 8: 139:4177  
REFERENCE 9: 139:4171  
REFERENCE 10: 138:399059

=> d his

(FILE 'HOME' ENTERED AT 14:58:12 ON 06 JUL 2003)  
SET COST OFF

FILE 'HCAPLUS' ENTERED AT 14:58:22 ON 06 JUL 2003

E WO2000-US23288/AP, PRN  
L1 1 S E3  
E US99-150743/AP, PRN  
L2 1 S E5  
E US2000-175347/AP, PRN  
L3 1 S E5  
L4 1 S L1-L3  
E SHUKLA D/AU  
L5 168 S E3-E12, E15, E16  
E ROSENBERG R/AU  
L6 2 S E3, E4  
E ROSENBERG R/AU  
L7 402 S E3, E8, E34, E40  
E SPEAR P/AU  
L8 142 S E3, E6, E9, E10  
L9 1 S L4 AND L5-L8  
SEL RN

FILE 'REGISTRY' ENTERED AT 15:02:48 ON 06 JUL 2003

L10 14 S E1-E14  
L11 6 S 67-68-5 OR 57-55-6 OR 67-63-0 OR 64-17-5 OR 112-80-1 OR 872-5  
L12 1 S 9050-30-0  
L13 14 S (70226-44-7 AND 7664-93-9)/CRN  
L14 3 S L13 AND (CA OR NA OR K)/ELS AND 3/NC  
L15 4 S L12, L14  
L16 7 S L10 NOT L11-L15  
L17 3 S L16 AND SQL/FA  
L18 4 S L16 NOT L17  
L19 1 S L18 AND UNSPECIFIED  
L20 3 S L18 NOT L19

FILE 'HCAPLUS' ENTERED AT 15:11:23 ON 06 JUL 2003

L21 703 S L5-L8 NOT L9

FILE 'HCAPLUS' ENTERED AT 15:11:31 ON 06 JUL 2003

SET SMARTSELECT ON  
L22 SEL L21 1- RN : 1245 TERMS  
SET SMARTSELECT OFF

FILE 'HCAPLUS' ENTERED AT 15:12:08 ON 06 JUL 2003

L24 703 S L21 OR L21  
SEL AN L24 1-200

L25 200 S E15-E406  
SEL AN L24 201-400  
L26 200 S E407-E803  
DEL SEL  
SEL AN L24 401-600  
L27 200 S E1-E400  
SEL AN L24 601-703  
L28 103 S E401-E606

FILE 'REGISTRY' ENTERED AT 15:15:14 ON 06 JUL 2003

FILE 'HCAPLUS' ENTERED AT 15:15:14 ON 06 JUL 2003

SET SMARTSELECT ON

L29 SEL L25 1- RN : 751 TERMS  
SET SMARTSELECT OFF

FILE 'REGISTRY' ENTERED AT 15:15:16 ON 06 JUL 2003

L30 751 S L29

FILE 'HCAPLUS' ENTERED AT 15:15:29 ON 06 JUL 2003

SET SMARTSELECT ON

L31 SEL L26 1- RN : 321 TERMS  
SET SMARTSELECT OFF

FILE 'REGISTRY' ENTERED AT 15:15:31 ON 06 JUL 2003

L32 322 S L31

FILE 'HCAPLUS' ENTERED AT 15:15:40 ON 06 JUL 2003

SET SMARTSELECT ON

L33 SEL L27 1- RN : 246 TERMS  
SET SMARTSELECT OFF

FILE 'REGISTRY' ENTERED AT 15:15:41 ON 06 JUL 2003

L34 246 S L33

FILE 'HCAPLUS' ENTERED AT 15:15:49 ON 06 JUL 2003

SET SMARTSELECT ON

L35 SEL L28 1- RN : 108 TERMS  
SET SMARTSELECT OFF

FILE 'REGISTRY' ENTERED AT 15:15:50 ON 06 JUL 2003

L36 108 S L35  
L37 1245 S L30,L32,L34,L36  
L38 1241 S L37 NOT L10  
L39 58 S L38 AND OC5/ES  
L40 188 S L38 AND S/ELS  
L41 333 S L38 AND UNSPECIFIED  
L42 144 S L41 NOT SQL/FA  
L43 8 S L42 AND SULFOTRANSFERASE  
L44 1 S L43 AND 3  
L45 184 S L40 NOT L41  
L46 54 S L45 AND L39  
L47 14 S L46 NOT SULFOAMINO  
L48 1 S L47 AND C12H21NO14S  
L49 130 S L45 NOT L46  
L50 96 S L49 NOT SQL/FA  
L51 4 S L39 NOT L46-L50  
L52 5 S L38 AND ?GLUC?/CNS NOT L39-L51  
L53 1 S L20 AND OC5/ES  
L54 STR  
L55 0 S L54  
L56 STR L54  
L57 0 S L56

L58 STR L56  
L59 0 S L58  
L60 16 S L58 FUL  
SAV L60 MAIER069/A  
L61 1 S L60 AND C12H21NO20S3  
SAV L61 MAIER069A/A  
E C6H13NO11S2/MF  
L62 9 S E3  
L63 3 S L62 NOT SULFOAMINO  
L64 2 S L63 NOT IDS/CI  
L65 1 S L64 AND 3  
L66 STR L58  
L67 9 S L66  
L68 224 S L66 FUL  
SAV L68 MAIER069B/A  
STR L66  
L69 0 S L69 SAM SUB=L68  
L70 4 S L69 FUL SUB=L68  
SAV L71 MAIER069C/A  
STR L69  
L72 30 S L72 FUL SUB=L68  
L73 SAV L73 MAIER069D/A  
L74 26 S L73 NOT L71,L65  
L75 1 S L74 AND C12H21NO20S3

FILE 'HCAPLUS' ENTERED AT 16:04:08 ON 06 JUL 2003

L76 5 S L61,L65,L75  
L77 2 S L76 AND (PY<=1999 OR PRY<=1999 OR AY<=1999)  
L78 19 S 3 OST  
L79 67 S 3 O () (SULFOTRANSFERASE OR SULPHOTRANSFERASE OR (SULFO OR SUL  
L80 70 S L78,L79  
L81 5 S L80 (L) 3A  
L82 4 S L80 (L) 3B  
L83 7 S L81,L82  
L84 21 S L80 AND L12  
L85 40 S L80 AND HEPARAN() (SULFATE OR SULPHATE)  
L86 40 S L84,L85  
L87 4 S 3OST#  
L88 42 S L83,L86,L87  
L89 42 S L80 AND L88  
L90 28 S L80 NOT L89  
L91 1 S L90 AND HERPES SIMPLEX  
SEL RN L89  
DEL SEL

FILE 'REGISTRY' ENTERED AT 16:12:03 ON 06 JUL 2003

FILE 'HCAPLUS' ENTERED AT 16:12:03 ON 06 JUL 2003

SET SMARTSELECT ON  
L92 SEL L89 1- RN : 4962 TERMS  
SET SMARTSELECT OFF

FILE 'REGISTRY' ENTERED AT 16:12:06 ON 06 JUL 2003

L93 4962 S L92  
L94 63 S L93 AND (?SULFOTRANSFERASE? OR ?SULPHOTRANSFERASE?)/CNS  
L95 61 S L94 AND (SULFOTRANSFERASE OR SULPHOTRANSFERASE)/INS.HP  
L96 2 S L94 NOT L95  
L97 47 S L95 AND 3  
L98 13 S L95 AND (3A OR 3B)  
L99 47 S L97,L98  
L100 14 S L95 NOT L99  
L101 41 S L99 AND (3 OR 3A OR 3B)/INS.HP  
L102 6 S L99 NOT L101



L103 2 S L102 NOT (SQL/FA OR STEROID)  
 L104 38 S L101 AND HEPAR?  
 L105 3 S L101 NOT L104  
 L106 2 S L105 AND 3 O  
 L107 19 S L104 AND 3 O  
 L108 1 S L107 NOT (CLONE OR MUS OR MOUSE)  
 L109 19 S L104 NOT L107  
 L110 2 S L19,L103  
 L111 909 S SULFOTRANSFERASE OR SULPHOTRANSFERASE  
 L112 846 S L111 NOT L94  
 L113 136 S L112 AND 3  
 L114 13 S L112 AND 3 O  
 L115 123 S L113 NOT L114  
 L116 0 S L112 AND (3A OR 3B)

FILE 'HCAPLUS' ENTERED AT 16:22:51 ON 06 JUL 2003

L117 34 S L110  
 L118 31 S L117 AND L78-L90  
 L120 15 S HEPARAN() (SULFATE OR SULPHATE) () (3 OR 3 O) () (SULFOTRANSFERASE  
 L121 73 S L78-L90,L117-L120  
 L122 6 S L121 AND ?HERPE?  
 E HERPES/CT  
 E E31+ALL  
 L123 2969 S E2  
 E E2+ALL  
 L124 4254 S E8  
 L125 9 S E6  
 E E6+ALL  
 L126 7223 S E9,E12  
 E E9+ALL  
 L127 10903 S E7,E9-E26/BI  
 L128 4250 S L12  
 L129 7432 S HEPARAN() (SULFATE OR SULPHATE)  
 L130 11444 S L123-L127  
 L131 39 S L130 AND L128  
 L132 82 S L130 AND L129  
 L133 1 S L77 AND L121  
 L134 1 S L77 AND L130  
 L135 2 S L77,L133,L134  
 E GLYCOPROTEIN/CT  
 L136 691 S E186,E187  
 L137 1024 S (GLYCOPROTEIN OR GP) (L)GD  
 L138 3 S L136,L137 AND L121  
 L139 672 S L136,L137 AND L130  
 L140 926 S L136,L137 AND (?HERPE? OR HSV?)  
 L141 708 S L139,L140 AND (PY<=1999 OR PRY<=1999 OR AY<=1999)  
 L142 0 S L141 AND (OVERSULFAT? OR OVERSULPHAT?)  
 E SULFATION/CT  
 E E3+ALL  
 L143 1 S L141 AND E3  
 L144 28 S L141 AND ?SACCHARIDE?  
 L145 130 S L5-L8 AND (?HERPE? OR HSV? OR L123-L127)  
 L146 6 S L145 AND ?SACCHARID?  
 L147 15 S L145 AND L128,L129  
 L148 4 S L145 AND L121  
 L149 19 S L146-L148  
 L150 15 S L149 AND (PY<=1999 OR PRY<=1999 OR AY<=1999)  
 L151 4 S L149 NOT L150  
 L152 20 S L150,L151,L135  
 L153 111 S L145 NOT L152  
 L154 10 S L152 AND (D OR GD)  
 L155 10 S L152 NOT L154  
 L156 163 S L129,L128 AND E3+NT

L157 2 S L156 AND L123-L127  
L158 2 S L156 AND (?HERPE? OR HSV?)  
L159 2 S L157,L158  
L160 11 S L159,L154

FILE 'REGISTRY' ENTERED AT 16:47:23 ON 06 JUL 2003

FILE 'HCAPLUS' ENTERED AT 16:48:24 ON 06 JUL 2003  
SEL HIT RN L160

FILE 'REGISTRY' ENTERED AT 16:50:00 ON 06 JUL 2003  
L161 4 S E1-E4

=> fil biosis

FILE 'BIOSIS' ENTERED AT 17:05:28 ON 06 JUL 2003  
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FILE COVERS 1969 TO DATE.  
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT  
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 2 July 2003 (20030702/ED)

=> d all tot

L190 ANSWER 1 OF 8 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
AN 2001:514668 BIOSIS  
DN PREV200100514668  
TI Portable **sulphotransferase** domain determines sequence  
specificity of **heparan sulphate 3-O**  
**-sulphotransferases**.  
AU Yabe, Tomio; Shukla, Deepak; Spear, Patricia G.;  
Rosenberg, Robert D.; Seeberger, Peter H.; Shworak, Nicholas W.  
(1)  
CS (1) Department of Medicine, Angiogenesis Research Center,  
Dartmouth-Hitchcock Medical Center, One Medical Center Drive, HB7504,  
Lebanon, NH, 03756: nicholas.shworak@dartmouth.edu USA  
SO Biochemical Journal, (1 October, 2001) Vol. 359, No. 1, pp. 235-241.  
print.  
ISSN: 0264-6021.  
DT Article  
LA English  
SL English  
AB 3-O-Sulphates are the rarest substituent of **heparan**  
**sulphate** and are therefore ideally suited to the selective  
regulation of biological activities. Individual isoforms of  
**heparan sulphate D-glucosaminyl 3-**  
**O-sulphotransferase (3-OST)** exhibit  
sequence-specific action, which creates **heparan sulphate**.  
structures with distinct biological functions. For example, 3-  
OST-1 preferentially generates binding sites for anti-thrombin,  
whereas 3-OST-3 isoforms create binding sites for the  
gD envelope protein of **herpes simplex virus 1**  
(HSV-1), which enables viral entry. 3-OST  
enzymes comprise a presumptive **sulphotransferase** domain and a  
divergent N-terminal region. To localize determinants of sequence  
specificity, we conducted domain swaps between cDNA species. The  
N-terminal region of 3-OST-1 was fused with the  
**sulphotransferase** domain of 3-OST-3A  
to generate N1-ST3A. Similarly, the N-terminal region of 3-  
OST-3A was fused to the **sulphotransferase**  
domain of 3-OST-1 to generate N3A-ST1. Wild-type and

chimaeric enzymes were transiently expressed in COS-7 cells and extracts were analysed for selective generation of binding sites for anti-thrombin. **3-OST-1** was 270-fold more efficient at forming anti-thrombin-binding sites than **3-OST-3A**, indicating its significantly greater selectivity for substrates that can be 3-O-sulphated to yield such sites. **N3A-ST1** was as active as **3-OST-1**, whereas the activity of **N1-ST3A** was as low as that of **3-OST-3A**. Analysis of Chinese hamster ovary cell transfectants revealed that only **3-OST-3A** and **N1-ST3A** generated **gD**-binding sites and conveyed susceptibility to infection by **HSV-1**. Thus sequence-specific properties of **3-OSTs** are defined by a self-contained **sulphotransferase** domain and are not directly influenced by the divergent N-terminal region.

- CC Cytology and Cytochemistry - Animal \*02506  
 Biochemical Studies - Carbohydrates \*10068  
 Enzymes - General and Comparative Studies; Coenzymes \*10802  
 Virology - Animal Host Viruses \*33506
- BC **Herpesviridae** 02612  
 Cercopithecidae 86205  
 Cricetidae 86310
- IT Major Concepts  
 Enzymology (Biochemistry and Molecular Biophysics)
- IT Chemicals & Biochemicals  
 3-O-sulfates; 3-O-sulfotransferase-1: amino-terminal domain, domain swapping, expression, **sulfotransferase** domain; 3-O-sulfotransferase-3-A: amino-terminal domain, domain swapping, expression, **sulfotransferase** domain; anti-coagulant; anti-thrombin; **gD** viral glycoprotein; **heparan sulfate**; **heparan sulphate**  
 3-O-sulphotransferases: expression, portable **sulphotransferase** domain, sequence specificity
- ORGN Super Taxa  
 Cercopithecidae: Primates, Mammalia, Vertebrata, Chordata, Animalia;  
 Cricetidae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia;  
**Herpesviridae: Animal Viruses, Viruses, Microorganisms**
- ORGN Organism Name  
 CHO cell line (Cricetidae): Chinese hamster ovary cells; COS-7 cell line (Cercopithecidae); **herpes simplex virus (Herpesviridae)**
- ORGN Organism Superterms  
 Animal Viruses; Animals; Chordates; Mammals; Microorganisms; Nonhuman Mammals; Nonhuman Primates; Nonhuman Vertebrates; Primates; Rodents; Vertebrates; Viruses
- RN 9000-94-6 (ANTI-THROMBIN)  
 9050-30-0 (HEPARAN SULFATE)
- L190 ANSWER 2 OF 8 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
 AN 2001:455646 BIOSIS  
 DN PREV200100455646  
 TI **Herpesviruses and heparan sulfate: An intimate relationship in aid of viral entry.**  
 AU **Shukla, Deepak; Spear, Patricia G. (1)**  
 CS (1) Department of Microbiology-Immunology, Northwestern University Medical School, 320 East Superior Street, Chicago, IL, 60611: p-spear@northwestern.edu USA  
 SO Journal of Clinical Investigation, (August, 2001) Vol. 108, No. 4, pp. 503-510. print.  
 ISSN: 0021-9738.  
 DT General Review  
 LA English  
 SL English  
 CC Cytology and Cytochemistry - General \*02502

Cytology and Cytochemistry - Human \*02508  
Biochemical Studies - General \*10060  
Biochemical Studies - Carbohydrates \*10068  
Virology - Animal Host Viruses \*33506  
Medical and Clinical Microbiology - Virology \*36006

BC **Herpesviridae** 02612  
Hominidae 86215

IT Major Concepts  
Biochemistry and Molecular Biophysics; Cell Biology; Infection

IT Diseases  
**herpesvirus** infection: clinical manifestations, pathogenesis,  
viral disease

IT Chemicals & Biochemicals  
**heparan sulfate**: viral entry receptor;  
**herpesvirus glycoproteins**: molecular interactions

IT Alternate Indexing  
**Herpesviridae** Infections (MeSH)

IT Miscellaneous Descriptors  
viral entry

ORGN Super Taxa  
**Herpesviridae: Animal Viruses, Viruses, Microorganisms**;  
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name  
**herpesviruses (Herpesviridae): pathogen; human (Hominidae):**  
host

ORGN Organism Superterms  
Animal Viruses; Animals; Chordates; Humans; Mammals; Microorganisms;  
Primates; Vertebrates; Viruses

RN 9050-30-0 (HEPARAN SULFATE)

L190 ANSWER 3 OF 8 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
AN 2001:84370 BIOSIS  
DN PREV200100084370  
TI Cell fusion induced by **herpes simplex** virus  
**glycoproteins** gB, gD, and gH-gL requires a gD  
receptor but not necessarily **heparan sulfate**.  
AU Pertel, Peter E.; Fridberg, Alina; Parish, Mary L.; Spear, Patricia  
G. (1)  
CS (1) Department of Microbiology-Immunology, Northwestern University Medical  
School, 320 East Superior Street, Room Ward 6-241, Chicago, IL, 60611:  
p-spear@northwestern.edu USA  
SO Virology, (January 5, 2001) Vol. 279, No. 1, pp. 313-324. print.  
ISSN: 0042-6822.  
DT Article  
LA English  
SL English  
AB To characterize cellular factors required for **herpes**  
**simplex** virus type 1 (HSV-1)-induced cell fusion, we  
used an efficient and quantitative assay relying on expression of  
HSV-1 **glycoproteins** in transfected cells. We showed the  
following: (1) Cell fusion depended not only on expression of four viral  
**glycoproteins** (gB, gD, and gH-gL), as previously shown,  
but also on expression of cell surface entry receptors specific for  
gD. (2) Cell fusion required expression of all four  
**glycoproteins** in the same cell. (3) **Heparan**  
**sulfate** was not required for cell fusion. (4) Coexpression of  
receptor with the four **glycoproteins** in the same cell reduced  
fusion activity, indicating that interaction of gD and receptor  
can limit polykaryocyte formation. Overall, the viral and cellular  
determinants of HSV-1-induced cell fusion are similar to those  
for viral entry, except that HSV-1 entry is significantly  
enhanced by binding of virus to cell surface **heparan**  
**sulfate**.

CC Biochemical Studies - Carbohydrates \*10068  
Cytology and Cytochemistry - Animal \*02506  
Biochemical Studies - Proteins, Peptides and Amino Acids \*10064  
Biophysics - Membrane Phenomena \*10508  
Virology - Animal Host Viruses \*33506  
Medical and Clinical Microbiology - Virology \*36006

BC **Herpesviridae 02612**  
Cricetidae 86310

IT Major Concepts  
Membranes (Cell Biology); Infection

IT Chemicals & Biochemicals  
gB: **glycoprotein**; gD: **glycoprotein**;  
gD receptor; gH-gL: **glycoprotein**; **heparan sulfate**: gD receptor

IT Miscellaneous Descriptors  
cell fusion

ORGN Super Taxa  
Cricetidae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia;  
**Herpesviridae: Animal Viruses, Viruses, Microorganisms**

ORGN Organism Name  
CHO-745 cell line (Cricetidae); CHO-K1 cell line (Cricetidae);  
**herpes simplex virus type 1 [HSV-1] (Herpesviridae): pathogen**

ORGN Organism Superterms  
Animal Viruses; Animals; Chordates; Mammals; Microorganisms; Nonhuman  
Mammals; Nonhuman Vertebrates; Rodents; Vertebrates; Viruses

RN **9050-30-0 (HEPARAN SULFATE)**

L190 ANSWER 4 OF 8 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
AN 1999:530618 BIOSIS  
DN PREV199900530618  
TI A novel role for 3-O-sulfated **heparan sulfate** in  
**herpes simplex virus 1** entry.  
AU **Shukla, Deepak**; Liu, Jian; Blaiklock, Peter; Shworak, Nicholas  
W.; Bai, Xiaomei; Esko, Jeffrey D.; Cohen, Gary H.; Eisenberg, Roselyn J.;  
**Rosenberg, Robert D.; Spear, Patricia G. (1)**  
CS (1) Department of Microbiology-Immunology, Northwestern University Medical  
School, Chicago, IL, 60611 USA  
SO Cell, (Oct. 1, 1999) Vol. 99, No. 1, pp. 13-22.  
ISSN: 0092-8674.  
DT Article  
LA English  
SL English  
AB **Herpes simplex virus type 1 (HSV-1)** binds to  
cells through interactions of viral **glycoproteins** gB and gC with  
**heparan sulfate** chains on cell surface proteoglycans.  
This binding is not sufficient for viral entry, which requires fusion  
between the viral envelope and cell membrane. Here, we show that  
**heparan sulfate** modified by a subset of the multiple  
**D-glucosaminyl 3-O-sulfotransferase**  
isoforms provides sites for the binding of a third viral  
**glycoprotein, gD**, and for initiation of **HSV-1**  
entry. We conclude that susceptibility of cells to **HSV-1** entry  
depends on (1) presence of **heparan sulfate** chains to  
which virus can bind and (2) 3-O-sulfation of specific glucosamine  
residues in **heparan sulfate** to generate gD  
-binding sites or the expression of other previously identified gD  
-binding receptors.

CC Medical and Clinical Microbiology - Virology \*36006  
Cytology and Cytochemistry - Animal \*02506  
Cytology and Cytochemistry - Human \*02508  
Biophysics - Membrane Phenomena \*10508  
Enzymes - General and Comparative Studies; Coenzymes \*10802  
Physiology and Biochemistry of Bacteria \*31000

BC **Herpesviridae 02612**  
 Animalia - Unspecified 33000  
 Hominidae 86215

IT Major Concepts  
 Enzymology (Biochemistry and Molecular Biophysics); Infection;  
 Membranes (Cell Biology)

IT Parts, Structures, & Systems of Organisms  
 viral envelope

IT Diseases  
**herpes simplex virus 1 infection: viral disease**

IT Chemicals & Biochemicals  
 gB [glycoprotein B]; gC [glycoprotein C];  
 gD [glycoprotein D]; D  
 -glucosaminyl 3-O-sulfotransferase;  
 3-O-sulfated heparan sulfate

IT Miscellaneous Descriptors  
 viral entry

ORGN Super Taxa  
 Animalia; **Herpesviridae: Animal Viruses, Viruses,**  
**Microorganisms;** Hominidae: Primates, Mammalia, Vertebrata,  
 Chordata, Animalia

ORGN Organism Name  
 animal (Animalia): host; **herpes simplex virus 1 (Herpesviridae):**  
**entry, pathogen;** human (Hominidae): host

ORGN Organism Superterms  
 Animal Viruses; Animals; Chordates; Humans; Mammals; Microorganisms;  
 Primates; Vertebrates; Viruses

RN **9050-30-0 (HEPARAN SULFATE)**

L190 ANSWER 5 OF 8 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
 AN 1997:393831 BIOSIS  
 DN PREV199799693034

TI **Glycoprotein D of herpes simplex**  
 virus (HSV) binds directly to HVEM, a member of the tumor  
 necrosis factor receptor superfamily and a mediator of HSV  
 entry.

AU Whitbeck, J. Charles (1); Peng, Charline; Lou, Huan; Xu, Ruliang; Willis,  
 Sharon H.; Ponce De Leon, Manuel; Peng, Tao; Nicola, Anthony V.;  
 Montgomery, Rebecca I.; Warner, Morgyn S.; Soulika, Athena M.; Spruce,  
 Lynn A.; Moore, William T.; Lambris, John D.; **Spear, Patricia G.**  
 ; Cohen, Gary H.; Eisenberg, Roselyn J.

CS (1) Sch. Dental Med., Univ. Pennsylvania, Philadelphia, PA 19104 USA

SO Journal of Virology, (1997) Vol. 71, No. 8, pp. 6083-6093.  
 ISSN: 0022-538X.

DT Article

LA English

AB **Glycoprotein D (gD)** is a structural  
 component of the **herpes simplex virus (HSV)**  
 envelope which is essential for virus entry into host cells. Chinese  
 hamster ovary (CHO-K1) cells are one of the few cell types which are  
 nonpermissive for the entry of many HSV strains. However, when  
 these cells are transformed with the gene for the **herpesvirus**  
 entry mediator (HVEM), the resulting cells, CHO-HVEM12, are permissive for  
 many HSV strains, such as HSV-1(KOS). By virtue of its  
 four cysteine-rich pseudorepeats, HVEM is a member of the tumor necrosis  
 factor receptor superfamily of proteins. Recombinant forms of gD  
 and HVEM, gD-1(306t) and HVEM(200t), respectively, were used to  
 demonstrate a specific physical interaction between these two proteins.  
 This interaction was dependent on native gD conformation but  
 independent of its N-linked **oligosaccharides**, as expected from  
 previous structure-function studies. Recombinant forms of gD  
 derived from HSV-1(KOS)rid1 and HSV-1(ANG) did not  
 bind to HVEM(200t), explaining the inability of these viruses to infect

CHOHVEM12 cells. A variant gD protein, gD-1(DELTA-290-299t), showed enhanced binding to HVEM(200t) relative to the binding of gD-1(306t). Competition studies showed that gD-1(DELTA-290-299t) and gD-1(306t) bound to the same region of HVEM(200t), suggesting that the differences in binding to HVEM are due to differences in affinity. These differences were also reflected in the ability of gD-1(DELTA-290-299t) but not gD-1(306t) to block HSV type 1 infection of CHO-HVEM12 cells. By gel filtration chromatography, the complex between gD-1(DELTA-290-299t) and HVEM(200t) had a molecular mass of 113 kDa and a molar ratio of 1:2. We conclude that HVEM interacts directly with gD, suggesting that HVEM is a receptor for virion gD and that the interaction between these proteins is a step in HSV entry into HVEM-expressing cells.

CC Cytology and Cytochemistry - Animal \*02506  
 Biochemical Studies - Proteins, Peptides and Amino Acids \*10064  
 Biochemical Studies - Carbohydrates \*10068  
 Biophysics - Molecular Properties and Macromolecules \*10506  
 In Vitro Studies, Cellular and Subcellular \*32600  
 Virology - Animal Host Viruses \*33506  
 Medical and Clinical Microbiology - Virology \*36006

BC **Herpesviridae** 02612  
 Cricetidae \*86310

IT Major Concepts  
 Biochemistry and Molecular Biophysics; Cell Biology; Infection; Microbiology

IT Miscellaneous Descriptors  
 BINDING; BIOCHEMISTRY AND BIOPHYSICS; **GD**;  
**GLYCOPROTEIN D**; **HERPESVIRUS** ENTRY MEDIATOR;  
**HSV**; HVEM; INFECTION; STRAIN-KOS; TUMOR NECROSIS FACTOR  
 RECEPTOR SUPERFAMILY MEMBER; VIRAL ENTRY

ORGN Super Taxa  
 Cricetidae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia;  
**Herpesviridae: Viruses**

ORGN Organism Name  
**herpes simplex virus (Herpesviridae)**; CHINESE HAMSTER OVARY  
 (Cricetidae): cell line; CHO-K1 (Cricetidae): cell line

ORGN Organism Superterms  
 animals; chordates; mammals; microorganisms; nonhuman mammals; nonhuman  
 vertebrates; rodents; vertebrates; viruses

L190 ANSWER 6 OF 8 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

AN 1989:95344 BIOSIS

DN BA87:49480

TI INITIAL INTERACTION OF **HERPES SIMPLEX** VIRUS WITH CELLS  
 IS BINDING TO **HEPARAN SULFATE**.

AU WUDUNN D; **SPEAR P G**

CS DEP. MICROBIOL./IMMUNOL., NORTHWESTERN UNIV. MED. SCH., CHICAGO, ILL.  
 60611.

SO J VIROL, (1989) 63 (1), 52-58.  
 CODEN: JOVIAM. ISSN: 0022-538X.

FS BA; OLD

LA English

AB We have shown that cell surface **heparan sulfate** serves as the initial receptor for both serotypes of **herpes simplex** virus (HSV). We found that virions could bind to heparin, a related glycosaminoglycan, and that heparin blocked virus adsorption. Agents known to bind to cell surface **heparan sulfate** blocked viral adsorption and infection. Enzymatic digestion of cell surface **heparan sulfate** but not of dermatan sulfate or chondroitin sulfate concomitantly reduced the binding of virus to the cells and rendered the cells resistant to infection. Although cell surface **heparan**

**sulfate** was required for infection by **HSV** types 1 and 2, the two serotypes may bind to **heparan sulfate** with different affinities or may recognize different structural features of **heparan sulfate**. Consistent with their broad host ranges, the two **HSV** serotypes use as primary receptors ubiquitous cell surface components known to participate in interactions with the extracellular matrix and with other cell surfaces.

CC Cytology and Cytochemistry - Human \*02508  
Biochemical Studies - Carbohydrates \*10068  
Biophysics - Membrane Phenomena 10508  
Virology - Animal Host Viruses \*33506  
Medical and Clinical Microbiology - Virology \*36006  
BC **Herpetoviridae** and/or **Herpesviridae** 02220  
Hominidae 86215  
IT Miscellaneous Descriptors  
HUMAN EXTRACELLULAR MATRIX  
RN 9050-30-0 (**HEPARAN SULFATE**)

L190 ANSWER 7 OF 8 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

AN 1988:408531 BIOSIS

DN BR35:71506

TI CELL SURFACE RECEPTOR FOR **HERPES SIMPLEX VIRUS** IS  
**HEPARAN SULFATE**.

AU WUDUNN D; **SPEAR P G**

CS UNIV. CHICAGO, CHICAGO, ILL. 60611.

SO SYMPOSIUM ON CELL BIOLOGY OF VIRUS ENTRY, REPLICATION AND PATHOGENESIS  
HELD AT THE 17TH ANNUAL UCLA (UNIVERSITY OF CALIFORNIA-LOS ANGELES)  
MEETING ON MOLECULAR AND CELLULAR BIOLOGY, TAOS, NEW MEXICO, USA, FEBRUARY  
28-MARCH 5, 1988. J CELL BIOCHEM SUPPL. (1988) 0 (12 PART C), 23.  
CODEN: JCBSD7.

DT Conference

FS BR; OLD

LA English

CC General Biology - Symposia, Transactions and Proceedings of Conferences;  
Congresses, Review Annuals 00520

Cytology and Cytochemistry - Human \*02508

Biochemical Studies - Proteins, Peptides and Amino Acids 10064

Biochemical Studies - Carbohydrates 10068

Biophysics - Membrane Phenomena \*10508

Metabolism - Carbohydrates \*13004

Metabolism - Proteins, Peptides and Amino Acids \*13012

Virology - Animal Host Viruses 33506

Medical and Clinical Microbiology - Virology \*36006

BC **Herpetoviridae** and/or **Herpesviridae** 02220

Hominidae 86215

IT Miscellaneous Descriptors

ABSTRACT HUMAN HEPARIN GLYCOSAMINOGLYCANS

RN 9005-49-6 (HEPARIN)

9050-30-0 (**HEPARAN SULFATE**)

L190 ANSWER 8 OF 8 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

AN 1983:288715 BIOSIS

DN BA76:46207

TI O LINKED OLIGO **SACCHARIDES** ARE ACQUIRED BY **HERPES**  
**SIMPLEX VIRUS GLYCO PROTEINS** IN THE GOLGI  
APPARATUS.

AU JOHNSON D C; **SPEAR P G**

CS DEP. MICROBIOL., UNIV. CHICAGO, CHICAGO, IL 60637.

SO CELL, (1983) 32 (3), 987-998.

CODEN: CELLB5. ISSN: 0092-8674.

FS BA; OLD

LA English

AB The O-linked **oligosaccharides** on mature forms of **herpes**



**simplex** virus type 1 (HSV1) **glycoproteins** were characterized, and were found to account largely for the lower electrophoretic mobilities of these forms relative to the mobilities of immature forms. Other posttranslational modifications of HSV1 **glycoproteins** (designated gB, gC, gD and gE) were related temporally to the discrete shifts in electrophoretic mobilities that signal acquisition of the O-linked **oligosaccharides**. Fatty acid acylation (principally of gE) could be detected just prior to the shift; conversion of high-mannose type N-linked **oligosaccharides** to the complex type occurred coincident with the shifts. The addition of O-linked **oligosaccharides** did not occur in cells treated with the ionophore monensin or in a ricin-resistant cell line defective in the processing of N-linked **oligosaccharides**. Evidently, extension of O-linked **oligosaccharide** chains on HSV1 **glycoproteins**, and probably also attachment of the first O-linked sugars, occurs as a late posttranslational modification in the Golgi apparatus. [Human laryngeal carcinoma Hep-2 cells were used in this study.]

CC Cytology and Cytochemistry - Human \*02508  
 Biochemical Methods - Nucleic Acids, Purines and Pyrimidines 10052  
 Biochemical Methods - Lipids 10056  
 Biochemical Studies - General 10060  
 Biochemical Studies - Proteins, Peptides and Amino Acids \*10064  
 Biochemical Studies - Lipids 10066  
 Biochemical Studies - Carbohydrates \*10068  
 Replication, Transcription, Translation 10300  
 Biophysics - Molecular Properties and Macromolecules \*10506  
 Biophysics - Membrane Phenomena 10508  
 Metabolism - Carbohydrates 13004  
 Metabolism - Lipids 13006  
 Metabolism - Proteins, Peptides and Amino Acids 13012  
 Respiratory System - General; Methods 16001  
 Pharmacology - Drug Metabolism; Metabolic Stimulators 22003  
 Neoplasms and Neoplastic Agents - Neoplastic Cell Lines 24005  
 Genetics of Bacteria and Viruses 31500  
 Tissue Culture, Apparatus, Methods and Media 32500  
 Virology - Animal Host Viruses \*33506  
 Chemotherapy - General; Methods; Metabolism 38502  
 Plant Physiology, Biochemistry and Biophysics - Chemical Constituents 51522  
 BC Animal Viruses - Unspecified 02200  
 Fungi - Unspecified 15000  
 Hominidae 86215  
 IT Miscellaneous Descriptors  
 POST TRANSLATIONAL MODIFICATION FATTY-ACID ACYLATION MONENSIN RICIN  
 METABOLIC-DRUG  
 RN 17090-79-8 (MONENSIN)

=> d his

(FILE 'HOME' ENTERED AT 14:58:12 ON 06 JUL 2003)  
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FILE 'HCAPLUS' ENTERED AT 14:58:22 ON 06 JUL 2003

E WO2000-US23288/AP, PRN  
 L1 1 S E3  
 E US99-150743/AP, PRN  
 L2 1 S E5  
 E US2000-175347/AP, PRN  
 L3 1 S E5  
 L4 1 S L1-L3  
 E SHUKLA D/AU

L5 168 S E3-E12,E15,E16  
E ROSENBERG R/AU  
L6 2 S E3,E4  
E ROSENBERG R/AU  
L7 402 S E3,E8,E34,E40  
E SPEAR P/AU  
L8 142 S E3,E6,E9,E10  
L9 1 S L4 AND L5-L8  
SEL RN

FILE 'REGISTRY' ENTERED AT 15:02:48 ON 06 JUL 2003

L10 14 S E1-E14  
L11 6 S 67-68-5 OR 57-55-6 OR 67-63-0 OR 64-17-5 OR 112-80-1 OR 872-5  
L12 1 S 9050-30-0  
L13 14 S (70226-44-7 AND 7664-93-9)/CRN  
L14 3 S L13 AND (CA OR NA OR K)/ELS AND 3/NC  
L15 4 S L12,L14  
L16 7 S L10 NOT L11-L15  
L17 3 S L16 AND SQL/FA  
L18 4 S L16 NOT L17  
L19 1 S L18 AND UNSPECIFIED  
L20 3 S L18 NOT L19

FILE 'HCAPLUS' ENTERED AT 15:11:23 ON 06 JUL 2003

L21 703 S L5-L8 NOT L9

FILE 'HCAPLUS' ENTERED AT 15:11:31 ON 06 JUL 2003

SET SMARTSELECT ON  
L22 SEL L21 1- RN : 1245 TERMS  
SET SMARTSELECT OFF

FILE 'HCAPLUS' ENTERED AT 15:12:08 ON 06 JUL 2003

L24 703 S L21 OR L21  
SEL AN L24 1-200  
L25 200 S E15-E406  
SEL AN L24 201-400  
L26 200 S E407-E803  
DEL SEL  
SEL AN L24 401-600  
L27 200 S E1-E400  
SEL AN L24 601-703  
L28 103 S E401-E606

FILE 'REGISTRY' ENTERED AT 15:15:14 ON 06 JUL 2003

FILE 'HCAPLUS' ENTERED AT 15:15:14 ON 06 JUL 2003

SET SMARTSELECT ON  
L29 SEL L25 1- RN : 751 TERMS  
SET SMARTSELECT OFF

FILE 'REGISTRY' ENTERED AT 15:15:16 ON 06 JUL 2003

L30 751 S L29

FILE 'HCAPLUS' ENTERED AT 15:15:29 ON 06 JUL 2003

SET SMARTSELECT ON  
L31 SEL L26 1- RN : 321 TERMS  
SET SMARTSELECT OFF

FILE 'REGISTRY' ENTERED AT 15:15:31 ON 06 JUL 2003

L32 322 S L31

FILE 'HCAPLUS' ENTERED AT 15:15:40 ON 06 JUL 2003

SET SMARTSELECT ON

L33 SEL L27 1- RN : 246 TERMS  
SET SMARTSELECT OFF

FILE 'REGISTRY' ENTERED AT 15:15:41 ON 06 JUL 2003  
L34 246 S L33

FILE 'HCAPLUS' ENTERED AT 15:15:49 ON 06 JUL 2003  
SET SMARTSELECT ON

L35 SEL L28 1- RN : 108 TERMS  
SET SMARTSELECT OFF

FILE 'REGISTRY' ENTERED AT 15:15:50 ON 06 JUL 2003

L36 108 S L35  
L37 1245 S L30,L32,L34,L36  
L38 1241 S L37 NOT L10  
L39 58 S L38 AND OC5/ES  
L40 188 S L38 AND S/ELS  
L41 333 S L38 AND UNSPECIFIED  
L42 144 S L41 NOT SQL/FA  
L43 8 S L42 AND SULFOTRANSFERASE  
L44 1 S L43 AND 3  
L45 184 S L40 NOT L41  
L46 54 S L45 AND L39  
L47 14 S L46 NOT SULFOAMINO  
L48 1 S L47 AND C12H21NO14S  
L49 130 S L45 NOT L46  
L50 96 S L49 NOT SQL/FA  
L51 4 S L39 NOT L46-L50  
L52 5 S L38 AND ?GLUC?/CNS NOT L39-L51  
L53 1 S L20 AND OC5/ES  
L54 STR  
L55 0 S L54  
L56 STR L54  
L57 0 S L56  
L58 STR L56  
L59 0 S L58  
L60 16 S L58 FUL  
SAV L60 MAIER069/A  
L61 1 S L60 AND C12H21NO20S3  
SAV L61 MAIER069A/A  
E C6H13NO11S2/MF  
L62 9 S E3  
L63 3 S L62 NOT SULFOAMINO  
L64 2 S L63 NOT IDS/CI  
L65 1 S L64 AND 3  
L66 STR L58  
L67 9 S L66  
L68 224 S L66 FUL  
SAV L68 MAIER069B/A  
STR L66  
L69 0 S L69 SAM SUB=L68  
L70 4 S L69 FUL SUB=L68  
SAV L71 MAIER069C/A  
L72 STR L69  
L73 30 S L72 FUL SUB=L68  
SAV L73 MAIER069D/A  
L74 26 S L73 NOT L71,L65  
L75 1 S L74 AND C12H21NO20S3

FILE 'HCAPLUS' ENTERED AT 16:04:08 ON 06 JUL 2003

L76 5 S L61,L65,L75  
L77 2 S L76 AND (PY<=1999 OR PRY<=1999 OR AY<=1999)  
L78 19 S 3 OST

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L79      67 S 3 O () (SULFOTRANSFERASE OR SULPHOTRANSFERASE OR (SULFO OR SUL
L80      70 S L78,L79
L81      5 S L80 (L) 3A
L82      4 S L80 (L) 3B
L83      7 S L81,L82
L84      21 S L80 AND L12
L85      40 S L80 AND HEPARAN() (SULFATE OR SULPHATE)
L86      40 S L84,L85
L87      4 S 3OST#
L88      42 S L83,L86,L87
L89      42 S L80 AND L88
L90      28 S L80 NOT L89
L91      1 S L90 AND HERPES SIMPLEX
          SEL RN L89
          DEL SEL

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FILE 'REGISTRY' ENTERED AT 16:12:03 ON 06 JUL 2003

FILE 'HCAPLUS' ENTERED AT 16:12:03 ON 06 JUL 2003

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          SET SMARTSELECT ON
L92      SEL L89 1- RN :    4962 TERMS
          SET SMARTSELECT OFF

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FILE 'REGISTRY' ENTERED AT 16:12:06 ON 06 JUL 2003

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L93      4962 S L92
L94      63 S L93 AND (?SULFOTRANSFERASE? OR ?SULPHOTRANSFERASE?)/CNS
L95      61 S L94 AND (SULFOTRANSFERASE OR SULPHOTRANSFERASE)/INS.HP
L96      2 S L94 NOT L95
L97      47 S L95 AND 3
L98      13 S L95 AND (3A OR 3B)
L99      47 S L97,L98
L100     14 S L95 NOT L99
L101     41 S L99 AND (3 OR 3A OR 3B)/INS.HP
L102     6 S L99 NOT L101
L103     2 S L102 NOT (SQL/FA OR STEROID)
L104     38 S L101 AND HEPAR?
L105     3 S L101 NOT L104
L106     2 S L105 AND 3 O
L107     19 S L104 AND 3 O
L108     1 S L107 NOT (CLONE OR MUS OR MOUSE)
L109     19 S L104 NOT L107
L110     2 S L19,L103
L111     909 S SULFOTRANSFERASE OR SULPHOTRANSFERASE
L112     846 S L111 NOT L94
L113     136 S L112 AND 3
L114     13 S L112 AND 3 O
L115     123 S L113 NOT L114
L116     0 S L112 AND (3A OR 3B)

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FILE 'HCAPLUS' ENTERED AT 16:22:51 ON 06 JUL 2003

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L117     34 S L110
L118     31 S L117 AND L78-L90
L120     15 S HEPARAN() (SULFATE OR SULPHATE) () (3 OR 3 O) () (SULFOTRANSFERASE
L121     73 S L78-L90,L117-L120
L122     6 S L121 AND ?HERPE?
          E HERPES/CT
          E E31+ALL
L123     2969 S E2
          E E2+ALL
L124     4254 S E8
L125     9 S E6
          E E6+ALL
L126     7223 S E9,E12

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      E E9+ALL
L127 10903 S E7,E9-E26/BI
L128 4250 S L12
L129 7432 S HEPARAN() (SULFATE OR SULPHATE)
L130 11444 S L123-L127
L131 39 S L130 AND L128
L132 82 S L130 AND L129
L133 1 S L77 AND L121
L134 1 S L77 AND L130
L135 2 S L77,L133,L134
      E GLYCOPROTEIN/CT
L136 691 S E186,E187
L137 1024 S (GLYCOPROTEIN OR GP) (L)GD
L138 3 S L136,L137 AND L121
L139 672 S L136,L137 AND L130
L140 926 S L136,L137 AND (?HERPE? OR HSV?)
L141 708 S L139,L140 AND (PY<=1999 OR PRY<=1999 OR AY<=1999)
L142 0 S L141 AND (OVERSULFAT? OR OVERSULPHAT?)
      E SULFATION/CT
      E E3+ALL
L143 1 S L141 AND E3
L144 28 S L141 AND ?SACCHARIDE?
L145 130 S L5-L8 AND (?HERPE? OR HSV? OR L123-L127)
L146 6 S L145 AND ?SACCHARID?
L147 15 S L145 AND L128,L129
L148 4 S L145 AND L121
L149 19 S L146-L148
L150 15 S L149 AND (PY<=1999 OR PRY<=1999 OR AY<=1999)
L151 4 S L149 NOT L150
L152 20 S L150,L151,L135
L153 111 S L145 NOT L152
L154 10 S L152 AND (D OR GD)
L155 10 S L152 NOT L154
L156 163 S L129,L128 AND E3+NT
L157 2 S L156 AND L123-L127
L158 2 S L156 AND (?HERPE? OR HSV?)
L159 2 S L157,L158
L160 11 S L159,L154

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FILE 'REGISTRY' ENTERED AT 16:47:23 ON 06 JUL 2003

FILE 'HCAPLUS' ENTERED AT 16:48:24 ON 06 JUL 2003  
 SEL HIT RN L160

FILE 'REGISTRY' ENTERED AT 16:50:00 ON 06 JUL 2003

L161 4 S E1-E4

FILE 'BIOSIS' ENTERED AT 16:50:51 ON 06 JUL 2003

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      E SHUKLA D/AU
L162 238 S E3-E11,E13
      E ROSENBERG R/AU
L163 457 S E3,E7
L164 156 S E31,E34
      E ROSENBURG R/AU
L165 8 S E3,E4
      E SPEAR P/AU
L166 175 S E3,E6,E11,E12,E13
L167 1021 S L162-L166
L168 168 S L167 AND (?HERPE? OR HSV? OR SIMPLEX)
L169 59 S 02612/BC AND L167
L170 168 S L168,L169
L171 16 S L170 AND (L12 OR L129)
L172 5 S L170 AND L121

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L173 0 S L61,L65,L75,L71  
L174 17 S L171,L172  
L175 11 S L174 AND PY<=1999  
L176 139 S L170 AND PY<=1999  
L177 5 S L170 AND ?SACCHARID?  
L178 4 S L176 AND L177  
L179 3 S L178 AND (GD OR D) (L) (GP OR GLYCOPROTEIN OR GLYCO PROTEIN)  
L180 2 S L179 NOT 75000/TI  
L181 7 S L175 AND (GP OR GLYCOPROTEIN OR GLYCO PROTEIN)  
L182 1 S L181 AND (GD OR D)  
L183 3 S L180,L182  
L184 6 S L181 NOT L183  
L185 9 S L174 NOT L177-L184  
SEL DN AN 3 4 5 8 9  
L186 5 S L185 AND E1-E10  
L187 8 S L183,L186  
L188 124 S L176 NOT L177-L187  
L189 8 S L187 AND L162-L188  
L190 8 S L189 AND (D OR GD OR GLYCOPROTEIN OR GLYCO PROTEIN OR ?SULFOT

FILE 'BIOSIS' ENTERED AT 17:05:28 ON 06 JUL 2003